BRAIN ENDOTHELIAL CELL EXPRESSION PATTERNS

This application claims the benefit of provisional applications serial numbers 60/403,390 filed August 15, 2002 and 60/458,978 filed April 1, 2003. The disclosures of each are expressly incorporated herein.

TECHNICAL FIELD OF THE INVENTION

This invention is related to the area of angiogenesis and anti-angiogenesis. In particular, it relates to genes which are characteristically expressed in brain glioma endothelial cells.

BACKGROUND OF THE INVENTION

Brain cancers represent an infrequent but deadly form of cancer that has seen little improvement in survivability over the last 30 years. Tumor excision followed by therapies relying on outdated cytotoxins and radiation inevitably results in a diminished quality of life. Gliomas represent the most common brain neoplasms with highly vascular and invasive characteristics defining gliomas as one of the most aggressive tumors known. Classifications of gliomas derive from both the cellular origin and staged aggressiveness. Derived from either astrocytes or oligodendrocytes, astrocytomas and oligodendrogliomas constitute the most common types of gliomas. As is common to other tumor type classifications, glioma increases in aggressiveness from the first to third stages of disease with stage IV, gliobastoma multiforme, being the most aggressive. Moreover, glioblastoma tumors constitute one of the most vascular tumors known.

Vascular permeability within the brain is limited in comparison to other organs. Similarily, the accessibility of brain malignancies to immune surveillance was thought to be restricted as well although more recent evidence suggests the brain is not wholly immunologically privileged. This so called "blood-brain barrier" is thought to derive primarily from a combination of brain-specific capillary transport systems and astrocyte-regulated cross-talk with the endothelial cell-based vasculature (for reviews, see Bart, J., Groen, H. J., Hendrikse, N. H., van der Graaf, W. T., Vaalburg, W., and de Vries, E. G. (2000). The blood-brain barrier

and oncology: new insights into function and modulation. Cancer Treat Rev *26*, 449-62.) The presence of tight junctions and an observed high electrical resistance both contribute to restricted transvascular molecular exchange. The existence of a therapeutically impermeable vasculature has resulted in a comparatively limited amount of work aimed at intervening in brain malignancies and other CNS diseases. Defining proteins preferentially expressed on either normal or diseased brain endothelial cells holds promise for expanding CNS therapeutic regimens.

The vascular microenvironment within gliomas has been studied primarily through morphological, circulatory and perfusion based experiments (for review see Vajkoczy, P., and Menger, M. D. (2000). Vascular microenvironment in gliomas. J Neurooncol *50*, 99-108; and Bart, J., Groen, H. J., Hendrikse, N. H., van der Graaf, W. T., Vaalburg, W., and de Vries, E. G. (2000). The blood-brain barrier and oncology: new insights into function and modulation. Cancer Treat Rev *26*, 449-62.) These studies demonstrate profound changes in vascualture architecture associated with tumor progression. Increased fenestrations, malperfusion, hyperpermeability, and reduced leukocyte-EC interaction are all phenotypic observations linked to glioma microvasculature Bernsen, H. J., Rijken, P. F., Oostendorp, T., and van der Kogel, A. J. (1995). Vascularity and perfusion of human gliomas xenografted in the athymic nude mouse. Br J Cancer *71*, 721-6; Vick, N. A., and Bigner, D. D. (1972). Microvascular abnormalities in virally-induced canine brain tumors. Structural bases for altered blood-brain barrier function. J Neurol Sci *17*, 29-39; and Hobbs, S. K., Monsky, W. L., Yuan, F., Roberts, W. G., Griffith, L., Torchilin, V. P., and Jain, R. K. (1998). Regulation of transport pathways in tumor vessels: role of tumor type and microenvironment. Proc Natl Acad Sci U S A *95*, 4607-12. It is also suggested that higher grade gliomas utilize intussuceptive capillary growth to a much larger degree than earlier staged gliomas that primarily utilize both sprouting an cooption to advance vessel growth. Vajkoczy, P., Schilling, L., Ullrich, A., Schmiedek, P., and Menger, M. D. (1998). Characterization of angiogenesis and microcirculation of high-grade glioma: an intravital multifluorescence microscopic approach in the athymic nude mouse. J Cereb Blood Flow Metab *18*, 510-20. The molecular characterization of glioma ECs has thus far been limited to the evaluation of common growth factors or previously defined brain EC transporters. Holash, J., Maisonpierre, P. C.,

Compton, D., Boland, P., Alexander, C. R., Zagzag, D., Yancopoulos, G. D., and Wiegand, S. J. (1999). Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF. Science *284*, 1994-8; Guerin, C., Wolff, J. E., Laterra, J., Drewes, L. R., Brem, H., and Goldstein, G. W. (1992). Vascular differentiation and glucose transporter expression in rat gliomas: effects of steroids. Ann Neurol *31*, 481-7.

To date, global gene expression profiles from endothelial cell-specific populations is limited to normal and tumorigenic colon tissue. St Croix, B., Rago, C., Velculescu, V., Traverso, G., Romans, K. E., Montgomery, E., Lal, A., Riggins, G. J., Lengauer, C., Vogelstein, B., and Kinzler, K. W. (2000). Genes expressed in human tumor endothelium. Science *289*, 1197-202. There is a need in the art for analysis of endothelial cells from other tissue, so that diagnostic and therapeutic for non-colonic tumors can be developed.

SUMMARY OF THE INVENTION

According to one embodiment of the invention a method is provided to aid in diagnosing glioma. An expression product of at least one gene in a first brain tissue sample suspected of being neoplastic is detected. The at least one gene is selected from the group consisting of signal sequence receptor, delta (translocon-associated protein delta); DC2 protein; KIAA0404 protein; symplekin; Huntingtin interacting protein I; plasmalemma vesicle associated protein; KIAA0726 gene product; latexin protein; transforming growth factor, beta 1; hypothetical protein FLJ22215; Rag C protein; hypothetical protein FLJ23471; N-myristoyltransferase 1; hypothetical protein dJ1181N3.1; ribosomal protein L27; secreted protein, acidic, cysteine-rich (osteonectin); Hs 111988; Hs 112238; laminin, alpha 5; protective protein for beta-galactosidase (galactosialidosis); Melanoma associated gene; Melanoma associated gene; E3 ubiquitin ligase SMURF1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; insulin-like growth factor binding protein 7; gene predicted from cDNA with a complete coding sequence; Thy-1 cell surface antigen; Hs 127824; GTP binding protein 2; Homo sapiens mRNA; cDNA DKFZp586D0918 (from clone DKFZp586D0918); cutaneous T-cell lymphoma-associated tumor antigen se20-4; differentially expressed nucleolar TGF-beta1 target protein (DENTT); dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive); smoothelin; integrin, alpha 5 (fibronectin receptor, alpha polypeptide); putative translation initiation factor;

retinoic acid induced 14; matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase); Lutheran blood group (Auberger b antigen included); stanniocalcin 2; nuclear factor (erythroid-derived 2)-like 2; protein tyrosine phosphatase, non-receptor type 1; integrin, alpha 10; collagen, type VI, alpha 2; chromosome 21 open reading frame 25; CDC37 (cell division cycle 37, S. cerevisiae, homolog); Hs 16450; Rho guanine nucleotide exchange factor (GEF) 7; creatine kinase, brain; hypothetical protein FLJ10297; hypothetical protein FLJ10350; TNF-induced protein; tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein); cofilin 1 (non-muscle); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); v-ets avian erythroblastosis virus E26 oncogene homolog 1; protease, cysteine, 1 (legumain); ribosomal protein L13; chromosome 22 open reading frame 5; zinc finger protein 144 (Mel-18); degenerative spermatocyte (homolog Drosophila; lipid desaturase); eukaryotic translation initiation factor 2C, 2; mitochondrial ribosomal protein L45; prostate tumor over expressed gene 1; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (14.5kD, B14.5a); glioma endothelial marker 1 precursor; NS1-binding protein; ribosomal protein L38; tuftelin-interacting protein; HLA class II region expressed gene KE2; translocase of inner mitochondrial membrane 17 homolog A (yeast); sudD (suppressor of bimD6, Aspergillus nidulans) homolog; heparan sulfate proteoglycan 2 (perlecan); SEC24 (S. cerevisiae) related gene family, member A; NADH dehydrogenase (ubiquinone) Fe-S protein 7 (20kD) (NADH-coenzyme Q reductase); DNA segment on chromosome X and Y (unique) 155 expressed sequence; annexin A2; Homo sapiens clone 24670 mRNA sequence; hypothetical protein; matrix metalloproteinase 10 (stromelysin 2); KIAA1049 protein; G protein-coupled receptor; hypothetical protein FLJ20401; matrix metalloproteinase 14 (membrane-inserted); KIAA0470 gene product; solute carrier family 29 (nucleoside transporters), member 1; stanniocalcin 1; stanniocalcin 1; stanniocalcin 1; tumor suppressor deleted in oral cancer-related 1; tumor suppressor deleted in oral cancer-related 1; apolipoprotein C-I; glutathione peroxidase 4 (phospholipid hydroperoxidase); Hs 272106; transcription factor binding to IGHM enhancer 3; hypothetical protein DKFZp762A227; hypothetical protein FLJ22362; CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32 and G344); PRO0628 protein; melanoma-associated antigen recognised by cytotoxic T lymphocytes; LOC88745;

Homo sapiens beta-1,3-galactosyltransferase-6 (B3GALT6) mRNA, complete cds; sprouty (Drosophila) homolog 4; sprouty (Drosophila) homolog 4; Homo sapiens mRNA; cDNA DKFZp434E1515 (from clone DKFZp434E1515); coactosin-like protein; hypothetical protein FLJ21865; Hs296234; KIAA0685 gene product; hypothetical protein FLJ10980; ribosomal protein L10; ribosomal protein S19; Hs 299251; Huntingtin interacting protein K; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 50374; Hs 311780; Hs 212191; v-akt murine thymoma viral oncogene homolog 2; Hs 328774; transducin-like enhancer of split 2, homolog of Drosophila E(sp1); KIAA1870 protein; ribosomal protein L10a; peptidylprolyl isomerase A (cyclophilin A); Hs 344224; hypothetical protein FLJ23239; hypothetical protein DKFZp761H221; KIAA1887 protein; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 701679; Homo sapiens cDNA FLJ30634 fis, clone CTONG2002453; Homo sapiens cDNA FLJ32203 fis, clone PLACE6003038, weakly similar to ZINC FINGER PROTEIN 84; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1035904; hypothetical protein LOC57333; myosin ID; plexin B2; lectin, galactoside-binding, soluble, 8 (galectin 8); double ring-finger protein, Dorfin; DKFZP434B168 protein; LIM domain binding 2; integrin beta 4 binding protein; synaptopodin; Hs 54828; insulin induced gene 1; acetyl LDL receptor; SREC; excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence); hypothetical protein FLJ22329; schwannomin-interacting protein 1; PTEN induced putative kinase 1; myosin X; Homo sapiens cDNA FLJ32424 fis, clone SKMUS2000954, moderately similar to Homo sapiens F-box protein Fbx25 (FBX25) 97; golgi phosphoprotein 1; splicing factor, arginine/serine-rich 6; laminin, gamma 3; cysteine-rich protein 2; U6 snRNA-associated Sm-like protein LSm7; hypothetical protein FLJ10707; Homo sapiens, Similar to RIKEN cDNA 2310012N15 gene, clone IMAGE:3342825, mRNA, partial cds; macrophage migration inhibitory factor (glycosylation-inhibiting factor); ubiquinol-cytochrome c reductase hinge protein; gap junction protein, alpha 1, 43kD (connexin 43); dihydropyrimidinase-like 3; aquaporin 1 (channel-forming integral protein, 28kD); protein expressed in thyroid; macrophage myristoylated alanine-rich C kinase substrate; procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI); protease, serine, 11 (IGF binding); 24-dehydrocholesterol reductase; collagen, type IV, alpha 2; profilin 1; apolipoprotein D; hyaluronoglucosaminidase 2; hypothetical protein

FLJ22678; quiescin Q6; ras homolog gene family, member A; ras homolog gene family, member A; plasminogen activator, urokinase; insulin-like growth factor binding protein 3; uridine phosphorylase; KIAA0638 protein; B7 homolog 3; lamin A/C; lamin A/C; lamin A/C; regulator of G-protein signalling 12; proteasome (prosome, macropain) 26S subunit, non-ATPase, 8; Homo sapiens, Similar to RIKEN cDNA 5730528L13 gene, clone MGC:17337 IMAGE:4213591, mRNA, complete cds; prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy); laminin, alpha 4; transcription elongation factor A (SII), 1; lectin, galactoside-binding, soluble, 3 binding protein; ribosomal protein S16; glycophorin C (Gerbich blood group); endothelin receptor type B; serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1; biglycan; small nuclear ribonucleoprotein polypeptide B"; transmembrane 4 superfamily member 2; TAF11 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 28 kD; lysyl oxidase-like 2; SRY (sex determining region Y)-box 4; SOX4 SRY (sex determining region Y)-box 4; SRY (sex determining region Y)-box 4; actin related protein 2/3 complex, subunit 2 (34 kD); Homo sapiens cDNA: FLJ23507 fis, clone LNG03128; hypothetical protein FLJ12442; Fas (TNFRSF6)-associated via death domain; mitogen-activated protein kinase kinase kinase 11; TEK tyrosine kinase, endothelial (venous malformations, multiple cutaneous and mucosal); insulin receptor; cell membrane glycoprotein, 110000M(r) (surface antigen); Homo sapiens cDNA FLJ11863 fis, clone HEMBA1006926; jagged 1 (Alagille syndrome); KIAA0304 gene product; pre-B-cell leukemia transcription factor 2; Homo sapiens cDNA FLJ31238 fis, clone KIDNE2004864; p53-induced protein; complement component 1, q subcomponent, receptor 1; complement component 1, q subcomponent, receptor 1; apolipoprotein E; chemokine (C-C motif) ligand 3; coagulation factor II (thrombin) receptor-like 3; coagulation factor III (thromboplastin, tissue factor); collagen, type I, alpha 1; collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant); C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9; cystatin C (amyloid angiopathy and cerebral hemorrhage); endoplasmic reticulum associated protein 140 kDa; ESTs; ESTs; ESTs, Highly similar to hypothetical protein FLJ10350 [Homo sapiens] [H.sapiens]; ESTs, Highly similar to ITB1_HUMAN Integrin beta-1 precursor (Fibronectin receptor beta subunit) (CD29) (Integrin VLA-4 beta subunit) [H.sapiens]; ESTs, Weakly similar to hypothetical protein FLJ20489

[Homo sapiens] [H.sapiens]; ESTs, Weakly similar to T17346 hypothetical protein DKFZp586O1624.1 - human (fragment) [H.sapiens]; ESTs, Weakly similar to T21371 hypothetical protein F25H8.3 - Caenorhabditis elegans [C.elegans]; eukaryotic translation initiation factor 4A, isoform 1; heme oxygenase (decycling) 1; Hermansky-Pudlak syndrome 4; Homo sapiens cDNA FLJ34888 fis, clone NT2NE2017332; Homo sapiens cDNA FLJ39848 fis, clone SPLEN2014669; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1977059; Homo sapiens, clone IMAGE:4845226, mRNA; hypothetical protein FLJ22329; hypothetical protein FLJ32205; hypothetical protein MGC4677; inhibin, beta B (activin AB beta polypeptide); insulin-like growth factor binding protein 5; junction plakoglobin; KIAA0620 protein; KIAA0943 protein; likely ortholog of rat vacuole membrane protein 1; Lysosomal-associated multispanning membrane protein-5; major histocompatibility complex, class I, B; major histocompatibility complex, class I, C; matrix Gla protein; matrix metalloproteinase 1 (interstitial collagenase); microtubule-associated protein 1 light chain 3 beta; nerve growth factor receptor (TNFR superfamily, member 16); ribosomal protein S9; ring finger protein 40; S100 calcium binding protein, beta (neural); sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B; SPARC-like 1 (mast9, hevin); tumor necrosis factor, alpha-induced protein 3; UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 3; UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5; von Willebrand factor; v-akt murine thymoma vial oncogene homolog 2; cyclin-dependent kinase (cdc2-like) 10; ortholog mouse myocytic induction/differentiation originator; brain-specific angiogenesis inhibitor 1 ; EGF-TM7 latrophilin-related protein; sema domain ; integrin, alpha 5 ; likely ortholog of mouse fibronectin type III; Lutheran blood group (Auberger b antigen included); SSR4, TRAPD; nerve growth factor receptor (TNFR superfamily, member 16); insulin-like growth factor binding protein; leukemia inhibitory factor; protein tyrosine phosphatase, nonreceptor type I; and Homo sapiens, clone IMAGE:3908182, mRNA, partial cds. Expression of the at least one gene in the first brain tissue sample is compared to expression of the at least one gene in a second brain tissue sample which is normal. Increased expression of the at least one gene in the first brain tissue sample relative to the second tissue sample identifies the first brain tissue sample as likely to be neoplastic.

According to another embodiment of the invention a method is provided of treating a glioma. Cells of the glioma are contacted with an antibody. The antibody specifically binds to an extracellular epitope of a protein selected from the group consisting of plasmalemma associated protein; KIAA0726 gene product; osteonectin: laminin, alpha 5; collagen, type IV, alpha 1; insulin-like growth factor binding protein 7; Thy-1 cell surface antigen; dysferlin, limb girdle muscular dystrophy 2B; integrin, alpha 5; matrix metalloproteinase 9; Lutjheran blood group, integrink, alpha 10, collagen, type VI, alpha 2; glioma endothelial marker 1 precursor; translocase of inner mitochondrial membrane 17 homolog A; heparan sulfate proteoglycan 2; annexin A2; matrix metalloproteinase 10; G protein-coupled receptor; matrix metalloproteinase 14; solute carrier family 29, member 1; CD59 antigen p18-20; KIAA 1870 protein; plexin B2; lectin, glactoside-binding, soluble, 8; integrin beta 4 binding protein; acetyl LDL receptor; laminin, gamma 3; macrophage migration inhibitory factor; gap junction p roein, alpha 1, 43 kD; aquaporin 1; protease, serine, 11; collagen, type IV, alpha 2; apolipoprotein D; plasminogen activator, urokinase; insulin-like growth factor binding protein 3; regulator of G-protein signaling 12; prosaposin; laminin, alpha 4; lectin, galactoside-binding, soluble, 3 binding protein; glycophorin C; endothelin receptor type B; biglycan; transmembrane 4 superfamilyh member 2; lysyl osidase-like 2; TEK tyrosine kinase, endothelial; insulin receptore; cell membrane glycoprotein, 110000M(r); jagged 1; plasmalemma vesicle associated protein; TEM13, Thy-1 cell surface antigen; coagulation factor II (thrombin) receptor-like 3; dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive); sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B; integrin, alpha 5 (fibronectin receptor, alpha polypeptide); likely ortholog of rat vacuole membrane protein 1; nerve growth factor receptor (TNFR superfamily, member 16); degenerative spermatocyte homolog, lipid desaturase (Drosophila); TEM1, endosialin; heme oxygenase (decycling) 1; G protein-coupled receptor; C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9; matrix metalloproteinase 14 (membrane-inserted); solute carrier family 29 (nucleoside transporters), member 1; likely ortholog of mouse embryonic epithelial gene 1; major histocompatibility complex, class I, C; likely ortholog of mouse fibronectin type III repeat containing protein 1; sprouty homolog 4 (Drosophila); KIAA0620 protein; coagulation factor III (thromboplastin, tissue factor); aquaporin 1 (channel-forming integral protein, 28kDa); major histocompatibility

complex, class I, B; Lysosomal-associated multispanning membrane protein-5; endothelin receptor type B; insulin receptor; complement component 1, q subcomponent, receptor 1; brain-specific angiogenesis inhibitor 1 ; EGF-TM7 latrophilin-related protein; sema domain ; integrin, alpha 5 ; likely ortholog of mouse fibronectin type III; Lutheran blood group (Auberger b antigen included); SSR4, TRAPD; nerve growth factor receptor (TNFR superfamily, member 16)and complement component 1, q subcomponent, receptor 1. Immune destruction of cells of the glioma is thereby triggered.

According to still another embodiment of the invention a method is provided for identifying a test compound as a potential anti-cancer or anti-glioma drug. A test compound is contacted with a cell which expresses at least one gene selected from the group consisting of: signal sequence receptor, delta (translocon-associated protein delta); DC2 protein; KIAA0404 protein; symplekin; Huntingtin interacting protein I; plasmalemma vesicle associated protein; KIAA0726 gene product; latexin protein; transforming growth factor, beta 1; hypothetical protein FLJ22215; Rag C protein; hypothetical protein FLJ23471; N-myristoyltransferase 1; hypothetical protein dJ1181N3.1; ribosomal protein L27; secreted protein, acidic, cysteine-rich (osteonectin); Hs 111988; Hs 112238; laminin, alpha 5; protective protein for beta-galactosidase (galactosialidosis); Melanoma associated gene; Melanoma associated gene; E3 ubiquitin ligase SMURF1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; insulin-like growth factor binding protein 7; gene predicted from cDNA with a complete coding sequence; Thy-1 cell surface antigen; Hs 127824; GTP binding protein 2; Homo sapiens mRNA; cDNA DKFZp586D0918 (from clone DKFZp586D0918); cutaneous T-cell lymphoma-associated tumor antigen se20-4; differentially expressed nucleolar TGF-beta1 target protein (DENTT); dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive); smoothelin; integrin, alpha 5 (fibronectin receptor, alpha polypeptide); putative translation initiation factor; retinoic acid induced 14; matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase); Lutheran blood group (Auberger b antigen included); stanniocalcin 2; nuclear factor (erythroid-derived 2)-like 2; protein tyrosine phosphatase, non-receptor type 1; integrin, alpha 10; collagen, type VI, alpha 2; chromosome 21 open reading frame 25; CDC37 (cell division cycle 37, S. cerevisiae, homolog); Hs 16450; Rho guanine nucleotide exchange factor

(GEF) 7; creatine kinase, brain; hypothetical protein FLJ10297; hypothetical protein FLJ10350; TNF-induced protein; tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein); cofilin 1 (non-muscle); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); v-ets avian erythroblastosis virus E26 oncogene homolog 1; protease, cysteine, 1 (legumain); ribosomal protein L13; chromosome 22 open reading frame 5; zinc finger protein 144 (Mel-18); degenerative spermatocyte (homolog Drosophila; lipid desaturase); eukaryotic translation initiation factor 2C, 2; mitochondrial ribosomal protein L45; prostate tumor over expressed gene 1; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (14.5kD, B14.5a); glioma endothelial marker 1 precursor; NS1-binding protein; ribosomal protein L38; tuftelin-interacting protein; HLA class II region expressed gene KE2; translocase of inner mitochondrial membrane 17 homolog A (yeast); sudD (suppressor of bimD6, Aspergillus nidulans) homolog; heparan sulfate proteoglycan 2 (perlecan); SEC24 (S. cerevisiae) related gene family, member A; NADH dehydrogenase (ubiquinone) Fe-S protein 7 (20kD) (NADH-coenzyme Q reductase); DNA segment on chromosome X and Y (unique) 155 expressed sequence; annexin A2; Homo sapiens clone 24670 mRNA sequence; hypothetical protein; matrix metalloproteinase 10 (stromelysin 2); KIAA1049 protein; G protein-coupled receptor; hypothetical protein FLJ20401; matrix metalloproteinase 14 (membrane-inserted); KIAA0470 gene product; solute carrier family 29 (nucleoside transporters), member 1; stanniocalcin 1; stanniocalcin 1; stanniocalcin 1; tumor suppressor deleted in oral cancer-related 1; tumor suppressor deleted in oral cancer-related 1; apolipoprotein C-I; glutathione peroxidase 4 (phospholipid hydroperoxidase); Hs 272106; transcription factor binding to IGHM enhancer 3; hypothetical protein DKFZp762A227; hypothetical protein FLJ22362; CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32 and G344); PRO0628 protein; melanoma-associated antigen recognised by cytotoxic T lymphocytes; LOC88745; Homo sapiens beta-1,3-galactosyltransferase-6 (B3GALT6) mRNA, complete cds; sprouty (Drosophila) homolog 4; sprouty (Drosophila) homolog 4; Homo sapiens mRNA; cDNA DKFZp434E1515 (from clone DKFZp434E1515); coactosin-like protein; hypothetical protein FLJ21865; Hs296234; KIAA0685 gene product; hypothetical protein FLJ10980; ribosomal protein L10; ribosomal protein S19; Hs 299251; Huntingtin interacting protein K; Homo sapiens

mRNA full length insert cDNA clone EUROIMAGE 50374; Hs 311780; Hs 212191; v-akt murine thymoma viral oncogene homolog 2; Hs 328774; transducin-like enhancer of split 2, homolog of Drosophila E(sp1); KIAA1870 protein; ribosomal protein L10a; peptidylprolyl isomerase A (cyclophilin A); Hs 344224; hypothetical protein FLJ23239; hypothetical protein DKFZp761H221; KIAA1887 protein; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 701679; Homo sapiens cDNA FLJ30634 fis, clone CTONG2002453; Homo sapiens cDNA FLJ32203 fis, clone PLACE6003038, weakly similar to ZINC FINGER PROTEIN 84; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1035904; hypothetical protein LOC57333; myosin ID; plexin B2; lectin, galactoside-binding, soluble, 8 (galectin 8); double ring-finger protein, Dorfin; DKFZP434B168 protein; LIM domain binding 2; integrin beta 4 binding protein; synaptopodin; Hs 54828; insulin induced gene 1; acetyl LDL receptor; SREC; excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence); hypothetical protein FLJ22329; schwannomin-interacting protein 1; PTEN induced putative kinase 1; myosin X; Homo sapiens cDNA FLJ32424 fis, clone SKMUS2000954, moderately similar to Homo sapiens F-box protein Fbx25 (FBX25) 97; golgi phosphoprotein 1; splicing factor, arginine/serine-rich 6; laminin, gamma 3; cysteine-rich protein 2; U6 snRNA-associated Sm-like protein LSm7; hypothetical protein FLJ10707; Homo sapiens, Similar to RIKEN cDNA 2310012N15 gene, clone IMAGE:3342825, mRNA, partial cds; macrophage migration inhibitory factor (glycosylation-inhibiting factor); ubiquinol-cytochrome c reductase hinge protein; gap junction protein, alpha 1, 43kD (connexin 43); dihydropyrimidinase-like 3; aquaporin 1 (channel-forming integral protein, 28kD); protein expressed in thyroid; macrophage myristoylated alanine-rich C kinase substrate; procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI); protease, serine, 11 (IGF binding); 24-dehydrocholesterol reductase; collagen, type IV, alpha 2; profilin 1; apolipoprotein D; hyaluronoglucosaminidase 2; hypothetical protein FLJ22678; quiescin Q6; ras homolog gene family, member A; ras homolog gene family, member A; plasminogen activator, urokinase; insulin-like growth factor binding protein 3; uridine phosphorylase; KIAA0638 protein; B7 homolog 3; lamin A/C; lamin A/C; lamin A/C; regulator of G-protein signalling 12; proteasome (prosome, macropain) 26S subunit, non-ATPase, 8; Homo sapiens, Similar to RIKEN cDNA 5730528L13 gene, clone MGC:17337

IMAGE:4213591, mRNA, complete cds; prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy); laminin, alpha 4; transcription elongation factor A (SII), 1; lectin, galactoside-binding, soluble, 3 binding protein; ribosomal protein S16; glycophorin C (Gerbich blood group); endothelin receptor type B; serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1; biglycan; small nuclear ribonucleoprotein polypeptide B"; transmembrane 4 superfamily member 2; TAF11 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 28 kD; lysyl oxidase-like 2; SRY (sex determining region Y)-box 4; SOX4 SRY (sex determining region Y)-box 4; SRY (sex determining region Y)-box 4; actin related protein 2/3 complex, subunit 2 (34 kD); Homo sapiens cDNA: FLJ23507 fis, clone LNG03128; hypothetical protein FLJ12442; Fas (TNFRSF6)-associated via death domain; mitogen-activated protein kinase kinase kinase 11; TEK tyrosine kinase, endothelial (venous malformations, multiple cutaneous and mucosal); insulin receptor; cell membrane glycoprotein, 110000M(r) (surface antigen); Homo sapiens cDNA FLJ11863 fis, clone HEMBA1006926; jagged 1 (Alagille syndrome); KIAA0304 gene product; pre-B-cell leukemia transcription factor 2; Homo sapiens cDNA FLJ31238 fis, clone KIDNE2004864; p53-induced protein; complement component 1, q subcomponent, receptor 1; complement component 1, q subcomponent, receptor 1; apolipoprotein E; chemokine (C-C motif) ligand 3; coagulation factor II (thrombin) receptor-like 3; coagulation factor III (thromboplastin, tissue factor); collagen, type I, alpha 1; collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant); C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9; cystatin C (amyloid angiopathy and cerebral hemorrhage); endoplasmic reticulum associated protein 140 kDa; ESTs; ESTs; ESTs, Highly similar to hypothetical protein FLJ10350 [Homo sapiens] [H.sapiens]; ESTs, Highly similar to ITB1_HUMAN Integrin beta-1 precursor (Fibronectin receptor beta subunit) (CD29) (Integrin VLA-4 beta subunit) [H.sapiens]; ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]; ESTs, Weakly similar to T17346 hypothetical protein DKFZp586O1624.1 - human (fragment) [H.sapiens]; ESTs, Weakly similar to T21371 hypothetical protein F25H8.3 - Caenorhabditis elegans [C.elegans]; eukaryotic translation initiation factor 4A, isoform 1; heme oxygenase (decycling) 1; Hermansky-Pudlak syndrome 4; Homo sapiens cDNA FLJ34888 fis, clone NT2NE2017332; Homo sapiens cDNA FLJ39848 fis,

clone SPLEN2014669; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1977059; Homo sapiens, clone IMAGE:4845226, mRNA; hypothetical protein FLJ22329; hypothetical protein FLJ32205; hypothetical protein MGC4677; inhibin, beta B (activin AB beta polypeptide); insulin-like growth factor binding protein 5; junction plakoglobin; KIAA0620 protein; KIAA0943 protein; likely ortholog of rat vacuole membrane protein 1; Lysosomal-associated multispanning membrane protein-5; major histocompatibility complex, class I, B; major histocompatibility complex, class I, C; matrix Gla protein; matrix metalloproteinase 1 (interstitial collagenase); microtubule-associated protein 1 light chain 3 beta; nerve growth factor receptor (TNFR superfamily, member 16); ribosomal protein S9; ring finger protein 40; S100 calcium binding protein, beta (neural); sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B; SPARC-like 1 (mast9, hevin); tumor necrosis factor, alpha-induced protein 3; UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 3; UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5; von Willebrand factor; v-akt murine thymoma vial oncogene homolog 2; cyclin-dependent kinase (cdc2-like) 10; ortholog mouse myocytic induction/differentiation originator; brain-specific angiogenesis inhibitor 1 ; EGF-TM7 latrophilin-related protein; sema domain ; integrin, alpha 5 ; likely ortholog of mouse fibronectin type III; Lutheran blood group (Auberger b antigen included); SSR4, TRAPD; nerve growth factor receptor (TNFR superfamily, member 16); insulin-like growth factor binding protein; leukemia inhibitory factor; protein tyrosine phosphatase, nonreceptor type I; and Homo sapiens, clone IMAGE:3908182, mRNA, partial cds. An expression product of the at least one gene is monitored. The test compound is identified as a potential anti-cancer drug if it decreases the expression of the at least one gene.

According to yet another embodiment of the invention a method is provided to aid in diagnosing glioma. An mRNA of at least one gene in a first brain tissue sample suspected of being neoplastic is detected. The at least one gene is identified by a tag selected from the group consisting of SEQ ID NO: 1-32. Expression of the at least one gene in the first brain tissue sample is compared to expression of the at least one gene in a second brain tissue sample which is normal. If increased expression of the at least one gene in the first brain tissue sample relative

to the second tissue sample if found, the first brain tissue sample is identified as likely to be neoplastic.

Another embodiment of the invention is a method of identifying a test compound as a potential anti-cancer or anti-glioma drug. A test compound is contacted with a cell. The cell expresses an mRNA of at least one gene identified by a tag selected from the group consisting of SEQ ID NO: 1-32. An mRNA of the at least one gene is monitored. The test compound is identified as a potential anti-cancer drug if it decreases the expression of at least one gene.

Still another embodiment of the invention is a method to induce an immune response to glioma. A protein or nucleic acid encoding a protein is administered to a mammal, preferably a human. The protein is selected from the group consisting of: signal sequence receptor, delta (translocon-associated protein delta); DC2 protein; KIAA0404 protein; symplekin; Huntingtin interacting protein I; plasmalemma vesicle associated protein; KIAA0726 gene product; latexin protein; transforming growth factor, beta 1; hypothetical protein FLJ22215; Rag C protein; hypothetical protein FLJ23471; N-myristoyltransferase 1; hypothetical protein dJ1181N3.1; ribosomal protein L27; secreted protein, acidic, cysteine-rich (osteonectin); Hs 111988; Hs 112238; laminin, alpha 5; protective protein for beta-galactosidase (galactosialidosis); Melanoma associated gene; Melanoma associated gene; E3 ubiquitin ligase SMURF1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; collagen, type IV, alpha 1; insulin-like growth factor binding protein 7; gene predicted from cDNA with a complete coding sequence; Thy-1 cell surface antigen; Hs 127824; GTP binding protein 2; Homo sapiens mRNA; cDNA DKFZp586D0918 (from clone DKFZp586D0918); cutaneous T-cell lymphoma-associated tumor antigen se20-4; differentially expressed nucleolar TGF-beta1 target protein (DENTT); dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive); smoothelin; integrin, alpha 5 (fibronectin receptor, alpha polypeptide); putative translation initiation factor; retinoic acid induced 14; matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase); Lutheran blood group (Auberger b antigen included); stanniocalcin 2; nuclear factor (erythroid-derived 2)-like 2; protein tyrosine phosphatase, non-receptor type 1; integrin, alpha 10; collagen, type VI, alpha 2; chromosome 21 open reading frame 25; CDC37 (cell division cycle 37, S. cerevisiae, homolog);

Hs 16450; Rho guanine nucleotide exchange factor (GEF) 7; creatine kinase, brain; hypothetical protein FLJ10297; hypothetical protein FLJ10350; TNF-induced protein; tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein); cofilin 1 (non-muscle); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated); v-ets avian erythroblastosis virus E26 oncogene homolog 1; protease, cysteine, 1 (legumain); ribosomal protein L13; chromosome 22 open reading frame 5; zinc finger protein 144 (Mel-18); degenerative spermatocyte (homolog Drosophila; lipid desaturase); eukaryotic translation initiation factor 2C, 2; mitochondrial ribosomal protein L45; prostate tumor over expressed gene 1; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (14.5kD, B14.5a); glioma endothelial marker 1 precursor; NS1-binding protein; ribosomal protein L38; tuftelin-interacting protein; HLA class II region expressed gene KE2; translocase of inner mitochondrial membrane 17 homolog A (yeast); sudD (suppressor of bimD6, Aspergillus nidulans) homolog; heparan sulfate proteoglycan 2 (perlecan); SEC24 (S. cerevisiae) related gene family, member A; NADH dehydrogenase (ubiquinone) Fe-S protein 7 (20kD) (NADH-coenzyme Q reductase); DNA segment on chromosome X and Y (unique) 155 expressed sequence; annexin A2; Homo sapiens clone 24670 mRNA sequence; hypothetical protein; matrix metalloproteinase 10 (stromelysin 2); KIAA1049 protein; G protein-coupled receptor; hypothetical protein FLJ20401; matrix metalloproteinase 14 (membrane-inserted); KIAA0470 gene product; solute carrier family 29 (nucleoside transporters), member 1; stanniocalcin 1; stanniocalcin 1; stanniocalcin 1; tumor suppressor deleted in oral cancer-related 1; tumor suppressor deleted in oral cancer-related 1; apolipoprotein C-I; glutathione peroxidase 4 (phospholipid hydroperoxidase); Hs 272106; transcription factor binding to IGHM enhancer 3; hypothetical protein DKFZp762A227; hypothetical protein FLJ22362; CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32 and G344); PRO0628 protein; melanoma-associated antigen recognised by cytotoxic T lymphocytes; LOC88745; Homo sapiens beta-1,3-galactosyltransferase-6 (B3GALT6) mRNA, complete cds; sprouty (Drosophila) homolog 4; sprouty (Drosophila) homolog 4; Homo sapiens mRNA; cDNA DKFZp434E1515 (from clone DKFZp434E1515); coactosin-like protein; hypothetical protein FLJ21865; Hs296234; KIAA0685 gene product; hypothetical protein FLJ10980; ribosomal protein L10; ribosomal

protein S19; Hs 299251; Huntingtin interacting protein K; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 50374; Hs 311780; Hs 212191; v-akt murine thymoma viral oncogene homolog 2; Hs 328774; transducin-like enhancer of split 2, homolog of Drosophila E(sp1); KIAA1870 protein; ribosomal protein L10a; peptidylprolyl isomerase A (cyclophilin A); Hs 344224; hypothetical protein FLJ23239; hypothetical protein DKFZp761H221; KIAA1887 protein; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 701679; Homo sapiens cDNA FLJ30634 fis, clone CTONG2002453; Homo sapiens cDNA FLJ32203 fis, clone PLACE6003038, weakly similar to ZINC FINGER PROTEIN 84; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1035904; hypothetical protein LOC57333; myosin ID; plexin B2; lectin, galactoside-binding, soluble, 8 (galectin 8); double ring-finger protein, Dorfin; DKFZP434B168 protein; LIM domain binding 2; integrin beta 4 binding protein; synaptopodin; Hs 54828; insulin induced gene 1; acetyl LDL receptor; SREC; excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence); hypothetical protein FLJ22329; schwannomin-interacting protein 1; PTEN induced putative kinase 1; myosin X; Homo sapiens cDNA FLJ32424 fis, clone SKMUS2000954, moderately similar to Homo sapiens F-box protein Fbx25 (FBX25) 97; golgi phosphoprotein 1; splicing factor, arginine/serine-rich 6; laminin, gamma 3; cysteine-rich protein 2; U6 snRNA-associated Sm-like protein LSm7 hypothetical protein FLJ10707; Homo sapiens, Similar to RIKEN cDNA 2310012N15 gene, clone IMAGE:3342825, mRNA, partial cds; macrophage migration inhibitory factor (glycosylation-inhibiting factor); ubiquinol-cytochrome c reductase hinge protein; gap junction protein, alpha 1, 43kD (connexin 43); dihydropyrimidinase-like 3; aquaporin 1 (channel-forming integral protein, 28kD); protein expressed in thyroid; macrophage myristoylated alanine-rich C kinase substrate; procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI); protease, serine, 11 (IGF binding); 24-dehydrocholesterol reductase; collagen, type IV, alpha 2; profilin 1; apolipoprotein D; hyaluronoglucosaminidase 2; hypothetical protein FLJ22678; quiescin Q6; ras homolog gene family, member A; ras homolog gene family, member A; plasminogen activator, urokinase; insulin-like growth factor binding protein 3; uridine phosphorylase; KIAA0638 protein; B7 homolog 3; lamin A/C; lamin A/C; lamin A/C; regulator of G-protein signalling 12; proteasome (prosome, macropain) 26S subunit, non-ATPase, 8; Homo sapiens, Similar to RIKEN cDNA

5730528L13 gene, clone MGC:17337 IMAGE:4213591, mRNA, complete cds; prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy); laminin, alpha 4; transcription elongation factor A (SII), 1; lectin, galactoside-binding, soluble, 3 binding protein; ribosomal protein S16; glycophorin C (Gerbich blood group); endothelin receptor type B; serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1; biglycan; small nuclear ribonucleoprotein polypeptide B"; transmembrane 4 superfamily member 2; TAF11 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 28 kD; lysyl oxidase-like 2; SRY (sex determining region Y)-box 4; SOX4 SRY (sex determining region Y)-box 4; SRY (sex determining region Y)-box 4; actin related protein 2/3 complex, subunit 2 (34 kD); Homo sapiens cDNA: FLJ23507 fis, clone LNG03128; hypothetical protein FLJ12442; Fas (TNFRSF6)-associated via death domain; mitogen-activated protein kinase kinase kinase 11; TEK tyrosine kinase, endothelial (venous malformations, multiple cutaneous and mucosal); insulin receptor; cell membrane glycoprotein, 110000M(r) (surface antigen); Homo sapiens cDNA FLJ11863 fis, clone HEMBA1006926; jagged 1 (Alagille syndrome); KIAA0304 gene product; pre-B-cell leukemia transcription factor 2; Homo sapiens cDNA FLJ31238 fis, clone KIDNE2004864; p53-induced protein; complement component 1, q subcomponent, receptor 1; complement component 1, q subcomponent, receptor 1; apolipoprotein E; chemokine (C-C motif) ligand 3; coagulation factor II (thrombin) receptor-like 3; coagulation factor III (thromboplastin, tissue factor); collagen, type I, alpha 1; collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant); C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9; cystatin C (amyloid angiopathy and cerebral hemorrhage); endoplasmic reticulum associated protein 140 kDa; ESTs; ESTs; ESTs, Highly similar to hypothetical protein FLJ10350 [Homo sapiens] [H.sapiens]; ESTs, Highly similar to ITB1_HUMAN Integrin beta-1 precursor (Fibronectin receptor beta subunit) (CD29) (Integrin VLA-4 beta subunit) [H.sapiens]; ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]; ESTs, Weakly similar to T17346 hypothetical protein DKFZp586O1624.1 - human (fragment) [H.sapiens]; ESTs, Weakly similar to T21371 hypothetical protein F25H8.3 - Caenorhabditis elegans [C.elegans]; eukaryotic translation initiation factor 4A, isoform 1; heme oxygenase (decycling) 1; Hermansky-Pudlak syndrome 4; Homo sapiens cDNA FLJ34888 fis, clone NT2NE2017332; Homo sapiens cDNA FLJ39848 fis,

clone SPLEN2014669; Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1977059; Homo sapiens, clone IMAGE:4845226, mRNA; hypothetical protein FLJ22329; hypothetical protein FLJ32205; hypothetical protein MGC4677; inhibin, beta B (activin AB beta polypeptide); insulin-like growth factor binding protein 5; junction plakoglobin; KIAA0620 protein; KIAA0943 protein; likely ortholog of rat vacuole membrane protein 1; Lysosomal-associated multispanning membrane protein-5; major histocompatibility complex, class I, B; major histocompatibility complex, class I, C; matrix Gla protein; matrix metalloproteinase 1 (interstitial collagenase); microtubule-associated protein 1 light chain 3 beta; nerve growth factor receptor (TNFR superfamily, member 16); ribosomal protein S9; ring finger protein 40; S100 calcium binding protein, beta (neural); sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B; SPARC-like 1 (mast9, hevin); tumor necrosis factor, alpha-induced protein 3; UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 3; UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5; von Willebrand factor; v-akt murine thymoma vial oncogene homolog 2; cyclin-dependent kinase (cdc2-like) 10; ortholog mouse myocytic induction/differentiation originator; brain-specific angiogenesis inhibitor 1 ; EGF-TM7 latrophilin-related protein; sema domain ; integrin, alpha 5 ; likely ortholog of mouse fibronectin type III; Lutheran blood group (Auberger b antigen included); SSR4, TRAPD; nerve growth factor receptor (TNFR superfamily, member 16); insulin-like growth factor binding protein; leukemia inhibitory factor; protein tyrosine phosphatase, nonreceptor type I; and Homo sapiens, clone IMAGE:3908182, mRNA, partial cds. An immune response to the protein is thereby induced.

The present invention thus provides the art with methods of diagnosing and treating gliomas and other brain tumors.

DETAILED DESCRIPTION OF THE INVENTION

Using SAGE (Serial Analysis of Gene Expression) profiling, this study was able to identify previously unrecognized, angiogenesis-specific markers that discriminate between non-proliferative and pathologic endothelial cells. We identified 255 human genes that were expressed at significantly higher levels in brain tumor endothelium than in normal brain

endothelium. See Table 1. We have named these markers GEMs (glioma endothelial markers). Any of the GEMs disclosed in any of the tables can be used in the methods of the present invention, according to the discretion of the skilled artisan.

ECs represent only a minor fraction of the total cells within normal or tumor tissues, and only those EC transcripts expressed at the highest levels would be expected to be represented in libraries constructed from unfractionated tissues. The genes described in the current study should therefore provide a valuable resource for basic and clinical studies of human brain angiogenesis in the future. Genes which have been identified as expressed more in glioma endothelial cells than in normal brain endothelial cells (GEMs) include those which correspond to tags shown in SEQ ID NOS: 1-32. The tags correspond to the segment of the cDNA that is 3' of the 3' most restriction endonuclease site for the restriction enzyme NlaIII which was used as the anchoring enzyme. The tag shown is the same strand as the mRNA. Other such genes are listed in Tables 1 and 2.

Table 1

StdTag	SEQ	LongTag	SEQ ID	Function
AAACCATTCT	1	AAACCATTCTCCTCCGC	256	
AAGGCAGGGA	2	AAGGCAGGGAGGGAGGG	257	
ACACAGCAAG	3	ACACAGCAAGACGAGAA	258	
AGCTGGAGTC	4	AGCTGGAGTCCTAGGCA	259	
AGCTGGCACC	5	AGCTGGCACCAGAGCCC	260	
ATAAATGAGG	6	ATAAATGAGGTAAGGTC	261	
CAAGCACCCC	7	CAAGCACCCCCGTTCCA	262	
CACTACCCAC	8	CACTACCCACCAGACGC	263	
CACTACTCAC	9	CACTACTCACCAGGCGC	264	
CCCACCTCCA	10	CCCACCTCCAGTCCAGC	265	
CCCGCCTCTT	11	CCCGCCTCTTCACGGGC	266	
CCTCAGATGT	12	CCTCAGATGTTTGAAAA	267	
CGCTACTCAC	13	CGCTACTCACCAGACGC	268	
CTAAGACCTC	14	CTAAGACCTCACCAGTC	269	
CTAAGACTTC	15	CTAAGACTTCACCGGTC	270	
GAGTGGGTGC	16	GAGTGGGTGCAGCCTCC	271	
GGGACAGCTG	17	GGGACAGCTGTCTGTGG	272	
GGGTTGGCTT	18	GGGTTGGCTTGAAACCA	273	
GTAAGTGTAC	19	GTAAGTGTACTGGAAGT	274	
GTAAGTGTAC	20	GTAAGTGTACTGGTAAG	275	
GTAGGGGTAA	21	GTAGGGGTAAAAGGAGG	276	
TAACCACTGC	22	TAACCACTGCACTTTCC	277	
TACTGCTCGG	23	TACTGCTCGGAGGTCGG	278	
TCAGGCTGAA	24	TCAGGCTGAAGTCAGGC	279	
TCCATACACC	25	TCCATACACCTATCCCC	280	
TCCTTTTAAA	26	TCCTTTTAAAACAAAAC	281	
TGATTAAGGT	27	TGATTAAGGTCGGCGCT	282	
TGGTATCACA	28	TGGTATCACACAAGGGG	283	
TGGTGTATGC	29	TGGTGTATGCATCGGGG	284	
TGTCACTGGG	30	TGTCACTGGGCAGGCGG	285	
TGTGGGAGGC	31	TGTGGGAGGCTGATGGG	286	
TTTAACGGCC	32	TTTAACGGCCGCGGTAC	287	

StdTag	SEQ	LongTag	SEQ ID	Function
GCTCTCTATG	33	GCTCTCTATGCTGACGT	288	signal sequence receptor, delta (translocon-associated protein delta)
AGAATGAAAC	34	AGAATGAAACTGCCGGG	289	DC2 protein
AAGTGGAATA	35	AAGTGGAATAAACTGCC	290	KIAA0404 protein
GATGACGACT	36	GATGACGACTCGGGGCT	291	symplekin; Huntingtin interacting protein I
CCCTTTCACA	37	CCCTTTCACACACACTT	292	plasmalemma vesicle associated protein
TCCTGGGGCA	38	TCCTGGGGCAGGGGCGG	293	KIAA0726 gene product
TCTATTGATG	39	TCTATTGATGTGTATGC	294	latexin protein
GGGGCTGTAT	40	GGGGCTGTATTTAAGGA	295	transforming growth factor, beta 1
CCCAGGACAC	41	CCCAGGACACCAGCTGG	296	hypothetical protein FLJ22215
GGAGCTGCTG	42	GGAGCTGCTGCTTGTGG	297	Rag C protein
TGGACAGCAG	43	TGGACAGCAGGGACCTG	298	hypothetical protein FLJ23471
TCTGGGAACA	44	TCTGGGAACAGGGACGG	299	N-myristoyltransferase 1
CCTGTGTATG	45	CCTGTGTATGTGTGTAA	300	hypothetical protein dJ1181N3.1
GGCAAGAAGA	46	GGCAAGAAGAAGATCGC	301	ribosomal protein L27
AAATGCTTGG	47	AAATGCTTGGAGGTGAA	302	secreted protein, acidic, cysteine-rich (osteonectin)
CTAAAAACCT	48	CTAAAAACCTTATGACA	303	secreted protein, acidic, cysteine-rich (osteonectin)
GAGCATTGCA	49	GAGCATTGCACCACCCG	304	secreted protein, acidic, cysteine-rich (osteonectin)
GGTGGACACG	50	GGTGGACACGGATCTGC	305	secreted protein, acidic, cysteine-rich (osteonectin)
GCTCCTGAGC	51	GCTCCTGAGCCCCGGCC	306	ESTs, Weakly similar to I65992 gene MLL protein [H.sapiens]
AAGAAGTGGA	52	AAGAAGTGGAGATTGTC	307	ESTs
TGGGAAGTGG	53	TGGGAAGTGGGCTCCTT	308	maternally expressed 3
ACTCGCTCTG	54	ACTCGCTCTGTGGAGGT	309	laminin, alpha 5
TTTCAGGGGA	55	TTTCAGGGGAGGGGGAA	310	protective protein for beta-galactosidase (galactosialidosis)
ACAACGTCCA	56	ACAACGTCCAGCTGGTG	311	Melanoma associated gene
GTCTCAGTGC	57	GTCTCAGTGCTGAGGCG	312	Melanoma associated gene
CCCCCTGCCC	58	CCCCCTGCCCCTCTGCC	313	E3 ubiquitin ligase SMURF1
AGAAACCACG	59	AGAAACCACGGAAATGG	314	collagen, type IV, alpha 1
GACCGCAGGA	60	GACCGCAGGAGGGCAGA	315	collagen, type IV, alpha 1
GTGCTACTTC	61	GTGCTACTTCTTCTTCT	316	collagen, type IV, alpha 1
GATAACTACA	62	GATAACTACATTACCTG	317	insulin-like growth factor binding protein 7
TGGCTGTGAC	63	TGGCTGTGACTGTGACT	318	gene predicted from cDNA with a complete coding sequence
GAGTGAGACC	64	GAGTGAGACCCAGGAGC	319	Thy-1 cell surface antigen
GAGTGGCTAC	65	GAGTGGCTACCCGCCGC	320	ESTs, Weakly similar to T28770 hypothetical protein W03D2.1 – Caenorhabditis elegans

StdTag	SEQ	LongTag	SEQ ID	Function
GACTCAGGGA	66	GACTCAGGGATTTGTTG	321	GTP binding protein 2
GTTATATGCC	67	GTTATATGCCCGGGAGA	322	Homo sapiens mRNA; cDNA DKFZp586D0918 (from clone
GAGGCGCTGC	68	GAGGCGCTGCTGCCACC	323	cutaneous T-cell lymphoma-associated tumor antigen se20-4; differentially expressed nucleolar TGF-beta1 target protein (DENTT)
GAGCTCTGAG	69	GAGCTCTGAGATCACCC	324	dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)
GCCAGCCAGT	70	GCCAGCCAGTGGCAAGC	325	Smoothelin
ATGGCAACAG	71	ATGGCAACAGATCTGGA	326	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)
AAGGAGTTAC	72	AAGGAGTTACACTAGTC	327	putative translation initiation factor
TCCCACAAGG	73	TCCCACAAGGCTGCTTG	328	retinoic acid induced 14
TAAATCCCCA	74	TAAATCCCCACTGGGAC	329	matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase)
CCCGCCCCCG	75	CCCGCCCCCGCCTTCCC	330	Lutheran blood group (Auberger b antigen included)
CCCGAGGCAG	76	CCCGAGGCAGAGTCGGG	331	stanniocalcin 2
CTACGTGATG	77	CTACGTGATGAAGATGG	332	nuclear factor (erythroid-derived 2)-like 2
ATGGGTTTGC	78	ATGGGTTTGCATTTTAG	333	protein tyrosine phosphatase, non-receptor type 1
GGCATTGTCT	79	GGCATTGTCTCTGTTTC	334	integrin, alpha 10
GTGCTAAGCG	80	GTGCTAAGCGGGCCCGG	335	collagen, type VI, alpha 2
ACCGTTTGCA	81	ACCGTTTGCATTCGAAA	336	chromosome 21 open reading frame 25
CAGCGCTGCA	82	CAGCGCTGCATTGACTC	337	CDC37 (cell division cycle 37, S. cerevisiae, homolog)
GAAGACACTT	83	GAAGACACTTGGTTTGA	338	ESTs
CGCTGGGCGT	84	CGCTGGGCGTCTGGGAC	339	Rho guanine nucleotide exchange factor (GEF) 7
CACCCCTGAT	85	CACCCCTGATGTTCGCC	340	creatine kinase, brain
GCCCCCCTGC	86	GCCCCCCTGCCCCGTGC	341	hypothetical protein FLJ10297
CCCCCTGCCC	87	CCCCCTGCCCTCGCCTG	342	hypothetical protein FLJ10350
AGCATAAAAA	88	AGCATAAAAATGCGTGC	343	TNF-induced protein
GGGCTGGACG	89	GGGCTGGACGGCTGCGT	344	tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
CTGCCAACTT	90	CTGCCAACTTCTAACCG	345	cofilin 1 (non-muscle)
AAGTGGATAG	91	AAGTGGATAGATACTTC	346	splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated)
CGTACTGAGC	92	CGTACTGAGCGCTTTGG	347	splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated)
CCGCTTACTC	93	CCGCTTACTCTGTTGGG	348	v-ets avian erythroblastosis virus E26 oncogene homolog 1

StdTag	SEQ	LongTag	SEQ ID	Function
GGGGCTTCTG	94	GGGGCTTCTGTAGCCCC	349	protease, cysteine, 1 (legumain)
CCCGTCCGGA	95	CCCGTCCGGAACGTCTA	350	ribosomal protein L13
AGTTCCACCA	96	AGTTCCACCAGAAAGCC	351	chromosome 22 open reading frame 5
GGCCTCCAGC	97	GGCCTCCAGCCACCCAC	352	zinc finger protein 144 (Mel-18)
GGAGGCTGAG	98	GGAGGCTGAGGTGGGAG	353	degenerative spermatocyte (homolog Drosophila; lipid desaturase)
CAGAGGCGTC	99	CAGAGGCGTCCGCAGGT	354	eukaryotic translation initiation factor 2C, 2
GACCAGCCTT	100	GACCAGCCTTCAGATGG	355	mitochondrial ribosomal protein L45
GAGGATGGTG	101	GAGGATGGTGTCCTGAG	356	prostate tumor over expressed gene 1
TCGTCGCAGA	102	TCGTCGCAGAAGGCGCT	357	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (14.5kD, B14.5a)
GGGGCTGCCC	103	GGGGCTGCCCAGCTGGA	358	tumor endothelial marker 1 precursor
CTGTACATAC	104	CTGTACATACTTTTTGG	359	NS1-binding protein
GCGACGAGGC	105	GCGACGAGGCGCGCTGG	360	ribosomal protein L38
GCCAAGTGAA	106	GCCAAGTGAACTGTGGC	361	tuftelin-interacting protein
AAGATAAACT	107	AAGATAAACTCTGGGCC	362	HLA class II region expressed gene KE2
GAGAGTGTAC	108	GAGAGTGTACTGGCACT	363	translocase of inner mitochondrial membrane 17 homolog A (yeast)
CCACTGCACT	109	CCACTGCACTCCGGCCT	364	sudD (suppressor of bimD6, Aspergillus nidulans) homolog
CCACCCTCAC	110	CCACCCTCACACACACA	365	heparan sulfate proteoglycan 2 (perlecan)
CAGACCATTG	111	CAGACCATTGTTTGATC	366	SEC24 (S. cerevisiae) related gene family, member A
GGGAGCTGCG	112	GGGAGCTGCGCCAACGG	367	NADH dehydrogenase (ubiquinone) Fe-S protein 7 (20kD) (NADH-coenzyme Q reductase)
GGGATTTCTG	113	GGGATTTCTGTGTCTGC	368	DNA segment on chromosome X and Y (unique) 155 expressed sequence
CTTCCAGCTA	114	CTTCCAGCTAACAGGTC	369	annexin A2
CAGAAACAGA	115	CAGAAACAGACTGGGGG	370	Homo saplens clone 24670 mRNA sequence
TCTGTGCTCA	116	TCTGTGCTCAGGAAGAG	371	hypothetical protein
TGCAATAGGT	117	TGCAATAGGTGAGAGAA	372	matrix metalloproteinase 10 (stromelysin 2)
ATGGCCAACT	118	ATGGCCAACTTCCACCT	373	KIAA1049 protein
TCACACAGTG	119	TCACACAGTGCCTGTCG	374	G protein-coupled receptor
GGCTTAGGAT	120	GGCTTAGGATGTGAATG	375	hypothetical protein FLJ20401
GGGAGGGGTG	121	GGGAGGGGTGGGGGTG	376	matrix metalloproteinase 14 (membrane-inserted)
GAAGTAGAAG	122	GAAGTAGAAGGTAAGGA	377	KIAA0470 gene product
CACCCTGTAC	123	CACCCTGTACAGTTGCC	378	solute carrier family 29 (nucleoside transporters), member 1
ATGTTTACAA	124	ATGTTTACAAGATGGCG	379	stanniocalcin 1
CAAACTGGTC	125	CAAACTGGTCTAGGTCA	380	stanniocalcin 1
GTAATGACAG	126	GTAATGACAGATGCAAG	381	stanniocalcin 1

StdTag	SEQ	LongTag	SEQ ID	Function
ACCTGCCGAC	127	ACCTGCCGACAGTGTTG	382	tumor suppressor deleted in oral cancer-related 1
TGATGCGCGC	128	TGATGCGCGCTTTGTTG	383	tumor suppressor deleted in oral cancer-related 1
TGGCCCCAGG	129	TGGCCCCAGGTGCCACC	384	apolipoprotein C-I
GCCTGCTGGG	130	GCCTGCTGGGCTTGGCT	385	glutathione peroxidase 4 (phospholipid hydroperoxidase)
TGCCTGTGGT	131	TGCCTGTGGTCCCAGCT	386	ESTs
GAGGGTATAC	132	GAGGGTATACTGAGGGG	387	transcription factor binding to IGHM enhancer 3
GGAGCCAGCT	133	GGAGCCAGCTGACCTGC	388	hypothetical protein DKFZp762A227
GAGCCTCAGG	134	GAGCCTCAGGTGCTCCC	389	hypothetical protein FLJ22362
TACTTCACAT	135	TACTTCACATACAGTGC	390	CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32 and G344)
TAATCCCAGC	136	TAATCCCAGCACTTTGG	391	PRO0628 protein
CACCTTCCAG	137	CACCTTCCAGCCCGGGG	392	melanoma-associated antigen recognised by cytotoxic T lymphocytes
GAGTCTGTTC	138	GAGTCTGTTCGTGACTC	393	LOC88745
GGATTTTGGT	139	GGATTTTGGTCTCTGTC	394	Homo sapiens beta-1,3-galactosyltransferase-6 (B3GALT6) mRNA,
TGCCTGTAGT	140	TGCCTGTAGTCCTAGTT	395	sprouty (Drosophila) homolog 4
TTACAAACAG	141	TTACAAACAGAAAAGCT	396	sprouty (Drosophila) homolog 4
TCTTCTTTCA	142	TCTTCTTTCAGAATGGG	397	Homo sapiens mRNA; cDNA DKFZp434E1515 (from clone
AGCACATTTG	143	AGCACATTTGATATAGC	398	coactosin-like protein
CAGGGCTCGC	144	CAGGGCTCGCGGTGCGGG	399	hypothetical protein FLJ21865
GCTGGTCCCA	145	GCTGGTCCCAGGGCCAG	400	ESTs, Weakly similar to T31613 hypothetical protein Y50E8A.i - Caenorhabditis elegans [C.elegans]
TCCACGCCCT	146	TCCACGCCCTTCCTGGC	401	KIAA0685 gene product
TTGCAATAGC	147	TTGCAATAGCAAAACCC	402	hypothetical protein FLJ10980
AGGGCTTCCA	148	AGGGCTTCCAATGTGCT	403	ribosomal protein L10
CTGGGTTAAT	149	CTGGGTTAATAAATTGC	404	ribosomal protein S19
AACCTGGGAG	150	AACCTGGGAGGTGGAGG	405	ESTs
GGCAACGTGG	151	GGCAACGTGGTAGAGGC	406	Huntingtin interacting protein K
GGATGCGCAG	152	GGATGCGCAGGGGAGGC	407	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 50374
CACCTGTAGT	153	CACCTGTAGTCCTAGCT	408	EST
GTGGTGGGCG	154	GTGGTGGGCGCCTGTAG	409	EST
GCAGGGTGGG	155	GCAGGGTGGGGAGGGG	410	v-akt murine thymoma viral oncogene homolog 2
CAAGCATCCC	156	CAAGCATCCCCGTTCCA	411	EST
TGGGGGCCGA	157	TGGGGGCCGATGGGCAG	412	transducin-like enhancer of split 2, homolog of Drosophila E(sp1)
TCAGTGTATT	158	TCAGTGTATTAAAACCC	413	KIAA1870 protein

StdTag	SEQ	LongTag	SEQ ID	Function
GGCAAGCCCC	159	GGCAAGCCCCAGCGCCT	414	ribosomal protein L10a
CCTAGCTGGA	160	CCTAGCTGGATTGCAGA	415	peptidylprolyl isomerase A (cyclophilin A)
GCAAAACCCT	161	GCAAAACCCTGCTCTCC	416	ESTs, Weakly similar to ubiquitous TPR motif, Y isoform [H.sapiens]
GCTGGTTCCT	162	GCTGGTTCCTGAGTGGC	417	hypothetical protein FLJ23239
GCACCTCAGC	163	GCACCTCAGCCAGGGGT	418	hypothetical protein DKFZp761H221
ACCAGCTGTC	164	ACCAGCTGTCCAGGGGC	419	KIAA1887 protein
TTTGAATCAG	165	TTTGAATCAGTGCTAGA	420	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 701679
AGACTAGGGG	166	AGACTAGGGGCCGGAGC	421	Homo sapiens cDNA FLJ30634 fis, clone CTONG2002453
AGCTCAGTGA	167	AGCTCAGTGAGAAGGGC	422	Homo sapiens cDNA FLJ32203 fis, clone PLACE6003038, weakly similar to ZINC FINGER PROTEIN 84
GGCCAACATT	168	GGCCAACATTTGGTCCA	423	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1035904
TTTGTGGGCA	169	TTTGTGGGCAGTCAGGC	424	hypothetical protein LOC57333
ATTGTAGACA	170	ATTGTAGACAATGAGGG	425	myosin ID
CCCTAGGTTG	171	CCCTAGGTTGGGCCCCT	426	plexin B2
AAATCACCAA	172	AAATCACCAATCAAGGC	427	lectin, galactoside-binding, soluble, 8 (galectin 8)
GGCTGCAGTC	173	GGCTGCAGTCTTCTTCC	428	double ring-finger protein, Dorfin
GTGGCAGGCG	174	GTGGCAGGCGCCTGTAG	429	DKFZP434B168 protein
TAAAGGCACA	175	TAAAGGCACAGTGGCTC	430	LIM domain binding 2
GGCTCCTGGC	176	GGCTCCTGGCTCTGGAC	431	integrin beta 4 binding protein
ATATTAGGAA	177	ATATTAGGAAGTCGGGG	432	Synaptopodin
GCTTCAGTGG	178	GCTTCAGTGGGGGAGAG	433	ESTs
TGATTAAAAC	179	TGATTAAAACAAGTTGC	434	insulin induced gene 1
AGCCACCACG	180	AGCCACCACGCCTGGTC	435	acetyl LDL receptor; SREC
GGCGGCTGCA	181	GGCGGCTGCAGAGCCTG	436	excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence)
TGTTTGGGGG	182	TGTTTGGGGGCTTTTAG	437	hypothetical protein FLJ22329
CCTGCCTCGT	183	CCTGCCTCGTAGTGAAG	438	schwannomin-interacting protein 1
AGGCCTGGGC	184	AGGCCTGGGCCTCTGCG	439	PTEN induced putative kinase 1
CAAAACTGTT	185	CAAAACTGTTTGTTGGC	440	myosin X
GAGAGGACAT	186	GAGAGGACATTGGAGGG	441	Homo sapiens cDNA FLJ32424 fis, clone SKMUS2000954, moderately similar to Homo sapiens F-box protein Fbx25 (FBX25) 97
GAGTTAGGCA	187	GAGTTAGGCACTTCCTG	442	golgi phosphoprotein 1
CCGTAGTGCC	188	CCGTAGTGCCTTTATGG	443	splicing factor, arginine/serine-rich 6

StdTag	SEQ	LongTag	SEQ ID	Function
CATAAACGGG	189	CATAAACGGGCACACCC	444	laminin, gamma 3
TCCCTGGCAG	190	TCCCTGGCAGAGGGCTT	445	cysteine-rich protein 2
GAGGCCATCC	191	GAGGCCATCCCCAACCC	446	U6 snRNA-associated Sm-like protein LSm7
TTGCCTGGGA	192	TTGCCTGGGATGCTGGT	447	hypothetical protein FLJ10707
CTGTCAGCGG	193	CTGTCAGCGGCTGCCCC	448	Homo sapiens, Similar to RIKEN cDNA 2310012N15 gene, clone IMAGE:3342825, mRNA, partial cds
AACGCGGCCA	194	AACGCGGCCAATGTGGG	449	macrophage migration inhibitory factor (glycosylation-inhibiting factor)
GGTTTGGCTT	195	GGTTTGGCTTAGGCTGG	450	ubiquinol-cytochrome c reductase hinge protein
GATTTTTGTG	196	GATTTTTGTGGTGTGGG	451	gap junction protein, alpha 1, 43kD (connexin 43)
GGCTGCCCTG	197	GGCTGCCCTGGGCAGCC	452	dihydropyrimidinase-like 3
ATGGCAACAG	198	ATGGCAACAGAAACCAA	453	aquaporin 1 (channel-forming integral protein, 28kD)
CGCTGTGGGG	199	CGCTGTGGGGTGCAGAC	454	protein expressed in thyroid
GGCAGCCAGA	200	GGCAGCCAGAGCTCCAA	455	macrophage myristoylated alanine-rich C kinase substrate
AGAGCAAACC	201	AGAGCAAACCGTAGTCC	456	procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)
TTTCCCTCAA	202	TTTCCCTCAAAGACTCT	457	protease, serine, 11 (IGF binding)
TCCCCGTGGC	203	TCCCCGTGGCTGTGGGG	458	24-dehydrocholesterol reductase
TTCTCCCAAA	204	TTCTCCCAAATACCGTT	459	collagen, type IV, alpha 2
GGCTGGGGGC	205	GGCTGGGGGCCAGGGCT	460	profilin 1
CCCTACCCTG	206	CCCTACCCTGTTACCTT	461	apolipoprotein D
TAGGACCCTG	207	TAGGACCCTGCAGGGGG	462	hyaluronoglucosaminidase 2
GTTTTTGCTT	208	GTTTTTGCTTCAGCGGC	463	hypothetical protein FLJ22678
CTTGATTCCC	209	CTTGATTCCCACGCTAC	464	quiescin Q6
GCTTGGCTCC	210	GCTTGGCTCCCAAAGGG	465	ras homolog gene family, member A
GGTGGCACTC	211	GGTGGCACTCAGTCTCT	466	ras homolog gene family, member A
ACCTGTGACC	212	ACCTGTGACCAGCACTG	467	plasminogen activator, urokinase
ACTGAGGAAA	213	ACTGAGGAAAGGAGCTC	468	insulin-like growth factor binding protein 3
TGCAGCGCCT	214	TGCAGCGCCTGCGGCCT	469	uridine phosphorylase
CTGGGGGGAA	215	CTGGGGGGAAGGGACTG	470	KIAA0638 protein
GTGCTATTCT	216	GTGCTATTCTGGGGCTG	471	B7 homolog 3
GGAGGGGGCT	217	GGAGGGGGCTTGAAGCC	472	lamin A/C
GTGCCTGAGA	218	GTGCCTGAGAGGCAGGC	473	lamin A/C
TCACAGGGTC	219	TCACAGGGTCCCCGGGG	474	lamin A/C
GGGCTCCCTG	220	GGGCTCCCTGGCCCTGG	475	regulator of G-protein signalling 12

StdTag	SEQ	LongTag	SEQ ID	Function
GCCCCAGGTA	221	GCCCCAGGTAGGGGGAC	476	proteasome (prosome, macropain) 26S subunit, non-ATPase, 8
GAAAGTGGCT	222	GAAAGTGGCTGTCCTGG	477	Homo sapiens, Similar to RIKEN cDNA 5730528L13 gene, clone MGC:17337 IMAGE:4213591, mRNA, complete cds
TCCCTGGCTG	223	TCCCTGGCTGTTGAGGC	478	prosaposin (variant Gaucher disease and variant metachromatic
ACAGAGCACA	224	ACAGAGCACAGCTGCCC	479	laminin, alpha 4
CTTTGCACTC	225	CTTTGCACTCTCCTTTG	480	transcription elongation factor A (SII), 1
ATGCTCCCTG	226	ATGCTCCCTGAGGAGCT	481	lectin, galactoside-binding, soluble, 3 binding protein
CCGTCCAAGG	227	CCGTCCAAGGGTCCGCT	482	ribosomal protein S16
GGGCCCCCTG	228	GGGCCCCCTGGGCAGTG	483	glycophorin C (Gerbich blood group)
CTTATGCTGC	229	CTTATGCTGCTGGTGCC	484	endothelin receptor type B
GGTTATTTTG	230	GGTTATTTTGGAGTGTA	485	serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1
GCCTGTCCCT	231	GCCTGTCCCTCCAAGAC	486	Biglycan
AAGATGAGGG	232	AAGATGAGGGGGCAGGC	487	small nuclear ribonucleoprotein polypeptide B"
CCAACAAGAA	233	CCAACAAGAATGCATTG	488	transmembrane 4 superfamily member 2
AAGGATGCGG	234	AAGGATGCGGTGATGGC	489	TAF11 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 28 kD
TGTCATCACA	235	TGTCATCACAGACACTT	490	lysyl oxidase-like 2
CAGGCTTTTT	236	CAGGCTTTTTGGCTTCC	491	SRY (sex determining region Y)-box 4
TCAAGTTCAC	237	TCAAGTTCACTGCCTGT	492	SOX4 SRY (sex determining region Y)-box 4
TCCCTGGGCA	238	TCCCTGGGCAGCTTCAG	493	SRY (sex determining region Y)-box 4
CAGGAGTTCA	239	CAGGAGTTCAAAGAAGG	494	actin related protein 2/3 complex, subunit 2 (34 kD)
CAGGTGGTTC	240	CAGGTGGTTCTGCCATC	495	Homo sapiens cDNA: FLJ23507 fis, clone LNG03128
GCCCACATCC	241	GCCCACATCCGCTGAGG	496	hypothetical protein FLJ12442
GCTGGGGTGG	242	GCTGGGGTGGGGGTGG	497	Fas (TNFRSF6)-associated via death domain
GACCTCCTGC	243	GACCTCCTGCCCTGGGG	498	mitogen-activated protein kinase kinase kinase 11
AGTGAATAAA	244	AGTGAATAAATGTCTTG	499	TEK tyrosine kinase, endothelial (venous malformations, multiple cutaneous and mucosal)
AAGGTTCTTC	245	AAGGTTCTTCTCAAGGG	500	insulin receptor
AGCCTGGACT	246	AGCCTGGACTGAGCCAC	501	cell membrane glycoprotein, 110000M(r) (surface antigen)
CAACCCAGAT	247	CAACCCAGATTGGGGTG	502	Homo sapiens cDNA FLJ11863 fis, clone HEMBA1006926
TGCTTCTGCC	248	TGCTTCTGCCACCCTGC	503	jagged 1 (Alagille syndrome)
CAGGTGACAA	249	CAGGTGACAAGGGCCCT	504	KIAA0304 gene product

StdTag	SEQ	LongTag	SEQ ID	Function
GGCCGGGGGC	250	GGCCGGGGGCAGTTCTC	505	pre-B-cell leukemia transcription factor 2
GTGCGCTAGG	251	GTGCGCTAGGGCCCCGG	506	Homo sapiens cDNA FLJ31238 fis, clone KIDNE2004864
AGGCTGTCCA	252	AGGCTGTCCAGGCTCTG	507	p53-induced protein
TGTTATGTCC	253	TGTTATGTCCATTTTGC	508	complement component 1, q subcomponent, receptor 1
TTTCCCAAAC	254	TTTCCCAAACTGTGAGG	509	complement component 1, q subcomponent, receptor 1
GGGGATGGGG	255	GGGGATGGGGTACTGCC	510	Homo sapiens, clone IMAGE:3908182, mRNA, partial cds

Table 2.

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink id	Cellular Component
33	Hs.102135	300090	SS	6748	endoplasmic reticulum, membrane
34	Hs.103180				
35	Hs.105850		KIAA0404	23130	
36	Hs.107019	602388	SPK	8189	cytoplasm, nucleoplasm
37	Hs.107125				membrane
38	Hs.107809		KIAA0726	9746	membrane
39	Hs.109276				
40	Hs.1103	190180	TGFB1	7040	
41	Hs.110443				
42	Hs.110950				
43	Hs.110964				
44	Hs.111039	160993	NMT1	4836	
45	Hs.11114		DJ1181N3	58476	
46	Hs.111611		RPL27	6155	intracellular, ribosome
47	Hs.111779	182120	SPARC	6678	basement membrane
48	Hs.111779	182120	SPARC	6678	basement membrane
49	Hs.111779	182120	SPARC	6678	basement membrane
50	Hs.111779	182120	SPARC	6678	basement membrane
51	Hs.111988				
52	Hs.112238				
53	Hs.112844				
54	Hs.11669	601033	LAMA5	3911	basement lamina
55	Hs.118126	256540	PPGB	5476	endoplasmic reticulum, lysosome

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink Id	Cellular Component
56	Hs.118893	600134	D2S448	7837	cellular_component unknown
57	Hs.118893	600134	D2S448	7837	cellular_component unknown
58	Hs.119120	605568	SMURF1	57154	intracellular
59	Hs.119129	120130	COL4A1	1282	collagen
60	Hs.119129	120130	COL4A1	1282	collagen
61	Hs.119129	120130	COL4A1	1282	collagen
62	Hs.119206	602867	IGFBP7	3490	extracellular
63	Hs.124				
64	Hs.125359	188230	THY1	7070	integral plasma membrane protein
65	Hs.127824				
66	Hs.13011		GTPBP2	54676	
67	Hs.13350				
68	Hs.136164				
69	Hs.143897	603009	DYSF	8291	plasma membrane
70	Hs.149098	602127	SMTN	6525	actin cytoskeleton
71	Hs.149609	135620	ITGA5	3678	cytoskeleton, extracellular matrix,
72	Hs.150580		SUI1	10209	cellular_component unknown
73	Hs.15165				
74	Hs.151738	120361	MMP9	4318	extracellular matrix, extracellular space
75	Hs.155048	111200	LU	4059	integral plasma membrane protein,
76	Hs.155223	603665	STC2	8614	
77	Hs.155396	600492	NFE2L2	4780	nucleus
78	Hs.155894	176885	PTPN1	5770	cytoplasm, soluble fraction
79	Hs.158237	604042	ITGA10	8515	cytoskeleton, extracellular matrix,
80	Hs.159263	120240	COL6A2	1292	extracellular matrix
81	Hs.16007				
82	Hs.160958	605065	CDC37	11140	
83	Hs.16450				
84	Hs.172813	605477	P85SPR	8874	
85	Hs.173724	123280	CKB	1152	cytoplasm
86	Hs.173739				
87	Hs.177596				
88	Hs.17839		GG2	25816	

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink id	Cellular Component
89	Hs.180338	603366	TNFRSF12	8718	integral plasma membrane protein,
90	Hs.180370	601442	CFL1	1072	cytoskeleton, nucleus
91	Hs.180610	605199	SFPQ	6421	nucleus
92	Hs.180610	605199	SFPQ	6421	nucleus
93	Hs.18063	164720	ETS1	2113	nucleus
94	Hs.18069	602620	PRSC1	5641	
95	Hs.180842	113703	RPL13	6137	cytosolic ribosome, intracellular
96	Hs.182626				
97	Hs.184669	600346	ZNF144	7703	nucleus
98	Hs.185973		DEGS	8560	endoplasmic reticulum, integral plasma
99	Hs.193053	606229	EIF2C2	27161	cellular_component unknown
100	Hs.19347		MRPL45	84311	mitochondrion
101	Hs.19555				
102	Hs.19561	602139	NDUFA7	4701	membrane fraction, mitochondrion,
103	Hs.195727	606064	TEM1	57124	extracellular matrix
104	Hs.197298		NS1	10625	spliceosome, transcription factor
105	Hs.2017	604182	RPL38	6169	60S ribosomal subunit, intracellular,
106	Hs.20225				
107	Hs.205736	605660	HKE2	10471	prefoldin
108	Hs.20716	605057	TIM17	10440	integral plasma membrane protein,
109	Hs.209061	603579	SUDD	8780	
110	Hs.211573	142461	HSPG2	3339	basement membrane, extracellular
111	Hs.211612		SEC24A	10802	COPII vesicle coat, endoplasmic
112	Hs.211914	601825	NDUFS7	4727	mitochondrion, NADH dehydrogenase
113	Hs.21595	312095	DXYS155E	8227	cellular_component unknown
114	Hs.217493	151740	ANXA2	302	plasma membrane, soluble fraction
115	Hs.21906				
116	Hs.22129				
117	Hs.2258	185260	MMP10	4319	extracellular matrix, extracellular space
118	Hs.227835				
119	Hs.23016		RDC1	57007	integral membrane protein, membrane
120	Hs.233955				
121	Hs.2399	600754	MMP14	4323	extracellular matrix, integral plasma
122	Hs.25132				

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink Id	Cellular Component
123	Hs.25450	602193	SLC29A1	2030	integral plasma membrane protein,
124	Hs.25590	601185	STC1	6781	
125	Hs.25590	601185	STC1	6781	
126	Hs.25590	601185	STC1	6781	
127	Hs.25664		DOC	10263	
128	Hs.25664		DOC	10263	
129	Hs.268571	107710	APOC1	341	
130	Hs.2706	138322	GPX4	2879	mitochondrion
131	Hs.272106				
132	Hs.274184	314310	TFE3	7030	nucleus
133	Hs.274453				
134	Hs.27836				
135	Hs.278573	107271	CD59	966	membrane fraction, plasma membrane
136	Hs.278941				
137	Hs.279869	604853	MAAT1	10573	
138	Hs.283636				
139	Hs.284284				
140	Hs.285814				
141	Hs.285814				
142	Hs.287830				
143	Hs.289092		CLP	23406	intracellular
144	Hs.29288				
145	Hs.296234				
146	Hs.296406				
147	Hs.29716				
148	Hs.29797	312173	RPL10	6134	60S ribosomal subunit, intracellular,
149	Hs.298262	603474	RPS19	6223	40S ribosomal subunit, intracellular, ribosome
150	Hs.299257				
151	Hs.300954				
152	Hs.302741				
153	Hs.311780				
154	Hs.312191				
155	Hs.326445	164731	AKT2	208	

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink id	Cellular Component
156	Hs.327884				
157	Hs.332173	601041	TLE2	7089	nucleus
158	Hs.334604		KIAA1870	85301	collagen
159	Hs.334895		RPL10A	4736	60S ribosomal subunit, intracellular,
160	Hs.342389	123840	PPIA	5478	cytoplasm
161	Hs.344224				
162	Hs.34516				
163	Hs.347297				
164	Hs.348428				
165	Hs.348967				
166	Hs.350065				
167	Hs.351706				
168	Hs.36353				
169	Hs.39619		LOC57333	57333	
170	Hs.39871	606539	MYO1D	4642	myosin
171	Hs.3989	604293	PLXNB2	23654	membrane
172	Hs.4082	606099	LGALS8	3964	extracellular space
173	Hs.48320		DORFIN	25897	centrosome
174	Hs.48604				
175	Hs.4980	603450	LDB2	9079	nucleus
176	Hs.5215	602912	ITGB4BP	3692	extrinsic plasma membrane protein,
177	Hs.5307				
178	Hs.54828				
179	Hs.56205	602055	INSIG1	3638	
180	Hs.57735		SREC	8578	membrane
181	Hs.59544	126380	ERCC1	2067	nucleus
182	Hs.61478				
183	Hs.61490				
184	Hs.6163		PINK1	65018	
185	Hs.61638				
186	Hs.61661				
187	Hs.6831				
188	Hs.6891	601944	SFRS6	6431	nucleus
189	Hs.69954	604349	LAMC3	10319	extracellular matrix, membrane

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink id	Cellular Component
190	Hs.70327	601183	CRIP2	1397	
191	Hs.70830		LOC51690	51690	nucleus, small nucleolar
192	Hs.7187				
193	Hs.7247				
194	Hs.73798	153620	MIF	4282	extracellular space
195	Hs.73818		UQCRH	7388	mitochondrial electron transport chain
196	Hs.74471	121014	GJA1	2697	connexon, integral plasma membrane
197	Hs.74566	601168	DPYSL3	1809	
198	Hs.74602	107776	AQP1	358	integral plasma membrane protein,
199	Hs.7486				
200	Hs.75061		MLP	65108	
201	Hs.75093	153454	PLOD	5351	endoplasmic reticulum
202	Hs.75111	602194	PRSS11	5654	extracellular space
203	Hs.75616				
204	Hs.75617	120090	COL4A2	1284	collagen, collagen type IV
205	Hs.75721	176610	PFN1	5216	actin cytoskeleton
206	Hs.75736	107740	APOD	347	extracellular space
207	Hs.76873	603551	HYAL2	8692	lysosome
208	Hs.7718				
209	Hs.77266	603120	QSCN6	5768	
210	Hs.77273	165390	ARHA	387	cytoskeleton
211	Hs.77273	165390	ARHA	387	cytoskeleton
212	Hs.77274	191840	PLAU	5328	extracellular space
213	Hs.77326	146732	IGFBP3	3486	extracellular space
214	Hs.77573	191730	UP	7378	
215	Hs.77864				
216	Hs.77873	605715	B7	80381	cellular_component unknown
217	Hs.77886	150330	LMNA	4000	lamin, nuclear lamina, nucleus
218	Hs.77886	150330	LMNA	4000	lamin, nuclear lamina, nucleus
219	Hs.77886	150330	LMNA	4000	lamin, nuclear lamina, nucleus
220	Hs.78281	602512	RGS12	6002	extrinsic plasma membrane protein,
221	Hs.78466		PSMD8	5714	19S proteasome regulatory particle
222	Hs.78531				

SEQ ID NO:	Unigene ID	OMIMID	gene symbol	locuslink Id	Cellular Component
223	Hs.78575	176801	PSAP	5660	extracellular space, integral membrane
224	Hs.78672	600133	LAMA4	3910	basement lamina
225	Hs.78869	601425	TCEA1	6917	nucleus
226	Hs.79339	600626	LGALS3BP	3959	extracellular space, membrane
227	Hs.80617	603675	RPS16	6217	40S ribosomal subunit, intracellular,
228	Hs.81994	110750	GYPC	2995	integral plasma membrane protein,
229	Hs.82002	131244	EDNRB	1910	integral plasma membrane protein,
230	Hs.82085	173360	SERPINE1	5054	
231	Hs.821	301870	BGN	633	extracellular matrix
232	Hs.82575	603520	SNRPB2	6629	nucleus, snRNP U2e
233	Hs.82749	300096	TM4SF2	7102	integral plasma membrane protein,
234	Hs.83126	600772	TAF2I	6882	nucleus, TFIID complex
235	Hs.83354		LOXL2	4017	extracellular space, membrane
236	Hs.83484	184430	SOX4	6659	nucleus
237	Hs.83484				
238	Hs.83484	184430	SOX4	6659	nucleus
239	Hs.83583	604224	ARPC2	10109	actin cytoskeleton, Arp2/3 protein
240	Hs.84063				
241	Hs.84753				
242	Hs.86131	602457	FADD	8772	cytoplasm
243	Hs.89449	600050	MAP3K11	4296	
244	Hs.89640	600221	TEK	7010	integral plasma membrane protein,
245	Hs.89695	147670	INSR	3643	integral plasma membrane protein,
246	Hs.90107		GP110	11047	integral plasma membrane protein,
247	Hs.9096				
248	Hs.91143	601920	JAG1	182	membrane
249	Hs.92236		KIAA0304	9757	nucleus
250	Hs.93728	176311	PBX2	5089	nucleus
251	Hs.9408				
252	Hs.96908		PIG11	9537	
253	Hs.97199	120577	C1QR	22918	integral plasma membrane protein,
254	Hs.97199	120577	C1QR	22918	integral plasma membrane protein,
255	Hs.99093				

Isolated and purified nucleic acids, according to the present invention are those which are not linked to those genes to which they are linked in the human genome. Moreover, they are not present in a mixture such as a library containing a multitude of distinct sequences from distinct genes. They may be, however, linked to other genes such as vector sequences or sequences of other genes to which they are not naturally adjacent. Tags disclosed herein, because of the way that they were made, represent sequences which are 3' of the 3' most restriction enzyme recognition site for the tagging enzyme used to generate the SAGE tags. In this case, the tags are 3' of the most 3' most NlaIII site in the cDNA molecules corresponding to mRNA. Nucleic acids corresponding to tags may be RNA, cDNA, or genomic DNA, for example. Such corresponding nucleic acids can be determined by comparison to sequence databases to determine sequence identities. Sequence comparisons can be done using any available technique, such as BLAST, available from the National Library of Medicine, National Center for Biotechnology Information. Tags can also be used as hybridization probes to libraries of genomic or cDNA to identify the genes from which they derive. Thus, using sequence comparisons or cloning, or combinations of these methods, one skilled in the art can obtain full-length nucleic acid sequences. Genes corresponding to tags will contain the sequence of the tag at the 3' end of the coding sequence or of the 3' untranslated region (UTR), 3' of the 3' most recognition site in the cDNA for the restriction endonuclease which was used to make the tags. The nucleic acids may represent either the sense or the anti-sense strand. Nucleic acids and proteins although disclosed herein with sequence particularity, may be derived from a single individual. Allelic variants which occur in the population of humans are included within the scope of such nucleic acids and proteins. Those of skill in the art are well able to identify allelic variants as being the same gene or protein. Given a nucleic acid, one of ordinary skill in the art can readily determine an open reading frame present, and consequently the sequence of a polypeptide encoded by the open reading frame and, using techniques well known in the art, express such protein in a suitable host. Proteins comprising such polypeptides can be the naturally occurring proteins, fusion proteins comprising exogenous sequences from other genes from humans or other species, epitope tagged polypeptides, etc. Isolated and purified proteins are not in a cell, and are separated from the normal cellular constituents, such as nucleic acids, lipids, etc. Typically the protein is purified to such an extent that it comprises the predominant

species of protein in the composition, such as greater than 50, 60 70, 80, 90, or even 95% of the proteins present.

Using the proteins according to the invention, one of ordinary skill in the art can readily generate antibodies which specifically bind to the proteins. Such antibodies can be monoclonal or polyclonal. They can be chimeric, humanized, or totally human. Any functional fragment or derivative of an antibody can be used including Fab, Fab', Fab2, Fab'2, and single chain variable regions. So long as the fragment or derivative retains specificity of binding for the endothelial marker protein it can be used. Antibodies can be tested for specificity of binding by comparing binding to appropriate antigen to binding to irrelevant antigen or antigen mixture under a given set of conditions. If the antibody binds to the appropriate antigen at least 2, 5, 7, and preferably 10 times more than to irrelevant antigen or antigen mixture then it is considered to be specific.

Techniques for making such partially to fully human antibodies are known in the art and any such techniques can be used. According to one particularly preferred embodiment, fully human antibody sequences are made in a transgenic mouse which has been engineered to express human heavy and light chain antibody genes. Multiple strains of such transgenic mice have been made which can produce different classes of antibodies. B cells from transgenic mice which are producing a desirable antibody can be fused to make hybridoma cell lines for continuous production of the desired antibody. See for example, Nina D. Russel, Jose R. F. Corvalan, Michael L. Gallo, C. Geoffrey Davis, Liise-Anne Pirofski. Production of Protective Human Antipneumococcal Antibodies by Transgenic Mice with Human Immunoglobulin Loci *Infection and Immunity* April 2000, p. 1820-1826; Michael L. Gallo, Vladimir E. Ivanov, Aya Jakobovits, and C. Geoffrey Davis. The human immunoglobulin loci introduced into mice: V (D) and J gene segment usage similar to that of adult humans *European Journal of Immunology* 30: 534-540, 2000; Larry L. Green. Antibody engineering via genetic engineering of the mouse: XenoMouse strains are a vehicle for the facile generation of therapeutic human monoclonal antibodies *Journal of Immunological Methods 231* 11-23, 1999; Yang X-D, Corvalan JRF, Wang P, Roy CM-N and Davis CG. Fully Human Anti-interleukin-8 Monoclonal Antibodies: Potential Therapeutics for the Treatment of Inflammatory Disease States. *Journal of Leukocyte Biology*

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Antibodies can also be made using phage display techniques. Such techniques can be used to isolate an initial antibody or to generate variants with altered specificity or avidity characteristics. Single chain Fv can also be used as is convenient. They can be made from vaccinated transgenic mice, if desired. Antibodies can be produced in cell culture, in phage, or in various animals, including but not limited to cows, rabbits, goats, mice, rats, hamsters, guinea pigs, sheep, dogs, cats, monkeys, chimpanzees, apes.

Antibodies can be labeled with a detectable moiety such as a radioactive atom, a chromophore, a fluorophore, or the like. Such labeled antibodies can be used for diagnostic techniques, either *in vivo*, or in an isolated test sample. Antibodies can also be conjugated, for example, to a pharmaceutical agent, such as chemotherapeutic drug or a toxin. They can be linked to a cytokine, to a ligand, to another antibody. Suitable agents for coupling to antibodies to achieve an anti-tumor effect include cytokines, such as interleukin 2 (IL-2) and Tumor Necrosis Factor (TNF); photosensitizers, for use in photodynamic therapy, including aluminum (III) phthalocyanine tetrasulfonate, hematoporphyrin, and phthalocyanine; radionuclides, such as iodine-131 (^{131}I), yttrium-90 (^{90}Y), bismuth-212 (^{212}Bi), bismuth-213 (^{213}Bi), technetium-99m (^{99m}Tc), rhenium-186 (^{186}Re), and rhenium-188 (^{188}Re); antibiotics, such as doxorubicin, adriamycin, daunorubicin, methotrexate, daunomycin, neocarzinostatin, and carboplatin; bacterial, plant, and other toxins, such as diphtheria toxin, pseudomonas exotoxin A,

staphylococcal enterotoxin A, abrin-A toxin, ricin A (deglycosylated ricin A and native ricin A), TGF-alpha toxin, cytotoxin from chinese cobra (naja naja atra), and gelonin (a plant toxin); ribosome inactivating proteins from plants, bacteria and fungi, such as restrictocin (a ribosome inactivating protein produced by *Aspergillus restrictus*), saporin (a ribosome inactivating protein from *Saponaria officinalis*), and RNase; tyrosine kinase inhibitors; ly207702 (a difluorinated purine nucleoside); liposomes containing antitumor agents (*e.g.*, antisense oligonucleotides, plasmids which encode for toxins, methotrexate, etc.); and other antibodies or antibody fragments, such as F(ab).

Those of skill in the art will readily understand and be able to make such antibody derivatives, as they are well known in the art. The antibodies may be cytotoxic on their own, or they may be used to deliver cytotoxic agents to particular locations in the body. The antibodies can be administered to individuals in need thereof as a form of passive immunization.

Characterization of extracellular regions for the cell surface and secreted proteins from the protein sequence is based on the prediction of signal sequence, transmembrane domains and functional domains. Antibodies are preferably specifically immunoreactive with membrane associated proteins, particularly to extracellular domains of such proteins or to secreted proteins. Such targets are readily accessible to antibodies, which typically do not have access to the interior of cells or nuclei. However, in some applications, antibodies directed to intracellular proteins may be useful as well. Moreover, for diagnostic purposes, an intracellular protein may be an equally good target since cell lysates may be used rather than a whole cell assay.

Computer programs can be used to identify extracellular domains of proteins whose sequences are known. Such programs include SMART software (Schultz et al., Proc. Natl. Acad. Sci. USA *95:* 5857-5864, 1998) and Pfam software (BaGEMan et al., Nucleic acids Res. *28:* 263-266, 2000) as well as PSORTII. Typically such programs identify transmembrane domains; the extracellular domains are identified as immediately adjacent to the transmembrane domains. Prediction of extracellular regions and the signal cleavage sites are only approximate. It may have a margin of error + or – 5 residues. Signal sequence can be predicted using three

different methods (Nielsen et al, *Protein Engineering* 10: 1-6 ,1997, Jagla et. al, Bioinformatics 16: 245-250 , 2000, Nakai, K and Horton, P. Trends in Biochem. Sci. 24:34-35, 1999) for greater accuracy. Similarly transmembrane (TM) domains can be identified by multiple prediction methods. (Pasquier, et. al, Protein Eng. 12:381-385, 1999, Sonnhammer et al., In Proc. of Sixth Int. Conf. on Intelligent Systems for Molecular Biology, p. 175-182 , Ed J. Glasgow, T. Littlejohn, F. Major, R. Lathrop, D. Sankoff, and C. Sensen Menlo Park, CA: AAAI Press, 1998 , Klein, et.al, Biochim. Biophys. Acta, 815:468, 1985, Nakai and Kanehisa Genomics, 14: 897-911 , 1992). In ambiguous cases, locations of functional domains in well characterized proteins are used as a guide to assign a cellular localization.

Putative functions or functional domains of novel proteins can be inferred from homologous regions in the database identified by BLAST searches (Altschul et. al. Nucleic Acid Res. 25: 3389-3402, 1997) and/or from a conserved domain database such as Pfam (BaGEMan et.al, Nucleic Acids Res. 27:260-262 1999) BLOCKS (Henikoff, et. al, Nucl. Acids Res. 28:228-230, 2000) and SMART (Ponting, et. al, Nucleic Acid Res. 27,229-232, 1999). Extracellular domains include regions adjacent to a transmembrane domain in a single transmembrane domain protein (out–in or type I class). For multiple transmembrane domains proteins, the extracellular domain also includes those regions between two adjacent transmembrane domains (in-out and out-in). For type II transmembrane domain proteins, for which the N-terminal region is cytoplasmic, regions following the transmembrane domain is generally extracellular. Secreted proteins on the other hand do not have a transmembrane domain and hence the whole protein is considered as extracellular.

Membrane associated proteins can be engineered to delete the transmembrane domains, thus leaving the extracellular portions which can bind to ligands. Such soluble forms of transmembrane receptor proteins can be used to compete with natural forms for binding to ligand. Thus such soluble forms act as inhibitors. and can be used therapeutically as anti-angiogenic agents, as diagnostic tools for the quantification of natural ligands, and in assays for the identification of small molecules which modulate or mimic the activity of a GEM:ligand complex.

Alternatively, the endothelial markers themselves can be used as vaccines to raise an immune response in the vaccinated animal or human. For such uses, a protein, or immunogenic fragment of such protein, corresponding to the intracellular, extracellular or secreted GEM of interest is administered to a subject. The immogenic agent may be provided as a purified preparation or in an appropriately expressing cell. The administration may be direct, by the delivery of the immunogenic agent to the subject, or indirect, through the delivery of a nucleic acid encoding the immunogenic agent under conditions resulting in the expression of the immunogenic agent of interest in the subject. The GEM of interest may be delivered in an expressing cell, such as a purified population of glioma endothelial cells or a populations of fused glioma endothelial and dendritic cells. Nucleic acids encoding the GEM of interest may be delivered in a viral or non-viral delivery vector or vehicle. Non-human sequences encoding the human GEM of interest or other mammalian homolog can be used to induce the desired immunologic response in a human subject. For several of the GEMs of the present invention, mouse, rat or other ortholog sequences are described herein or can be obtained from the literature or using techniques well within the skill of the art.

Endothelial cells can be identified using the markers which are disclosed herein as being endothelial cell specific. These include the human markers identified by SEQ ID NOS: 1-510. Antibodies specific for such markers can be used to identify such cells, by contacting the antibodies with a population of cells containing some endothelial cells. The presence of cross-reactive material with the antibodies identifies particular cells as endothelial. Similarly, lysates of cells can be tested for the presence of cross-reactive material. Any known format or technique for detecting cross-reactive material can be used including, immunoblots, radioimmunoassay, ELISA, immunoprecipitation, and immunohistochemistry. In addition, nucleic acid probes for these markers can also be used to identify endothelial cells. Any hybridization technique known in the art including Northern blotting, RT-PCR, microarray hybridization, and in situ hybridization can be used.

One can identify glioma endothelial cells for diagnostic purposes, testing cells suspected of containing one or more GEMs. One can test both tissues and bodily fluids of a subject. For

example, one can test a patient's blood for evidence of intracellular and membrane associated GEMs, as well as for secreted GEMs. Intracellular and/or membrane associated GEMs may be present in bodily fluids as the result of high levels of expression of these factors and/or through lysis of cells expressing the GEMs.

Populations of various types of endothelial cells can also be made using the antibodies to endothelial markers of the invention. The antibodies can be used to purify cell populations according to any technique known in the art, including but not limited to fluorescence activated cell sorting. Such techniques permit the isolation of populations which are at least 50, 60, 70, 80, 90, 92, 94, 95, 96, 97, 98, and even 99 % the type of endothelial cell desired, whether normal, tumor, or pan-endothelial. Antibodies can be used to both positively select and negatively select such populations. Preferably at least 1, 5, 10, 15, 20, or 25 of the appropriate markers are expressed by the endothelial cell population.

Populations of endothelial cells made as described herein, can be used for screening drugs to identify those suitable for inhibiting the growth of tumors by virtue of inhibiting the growth of the tumor vasculature.

Populations of endothelial cells made as described herein, can be used for screening candidate drugs to identify those suitable for modulating angiogenesis, such as for inhibiting the growth of tumors by virtue of inhibiting the growth of endothelial cells, such as inhibiting the growth of the tumor or other undesired vasculature, or alternatively, to promote the growth of endothelial cells and thus stimulate the growth of new or additional large vessel or microvasculature.

Inhibiting the growth of endothelial cells means either regression of vasculature which is already present, or the slowing or the absence of the development of new vascularization in a treated system as compared with a control system. By stimulating the growth of endothelial cells, one can influence development of new (neovascularization) or additional vasculature development (revascularization). A variety of model screening systems are available in which to

test the angiogenic and/or anti-angiogenic properties of a given candidate drug. Typical tests involve assays measuring the endothelial cell response, such as proliferation, migration, differentiation and/or intracellular interaction of a given candidate drug. By such tests, one can study the signals and effects of the test stimuli. Some common screens involve measurement of the inhibition of heparanase, endothelial tube formation on Matrigel, scratch induced motility of endothelial cells, platelet-derived growth factor driven proliferation of vascular smooth muscle cells, and the rat aortic ring assay (which provides an advantage of capillary formation rather than just one cell type).

Drugs can be screened for the ability to mimic or modulate, inhibit or stimulate, growth of tumor endothelium cells and/or normal endothelial cells. Drugs can be screened for the ability to inhibit tumor endothelium growth but not normal endothelium growth or survival. Similarly, human cell populations, such as normal endothelium populations or glioma endothelial cell populations, can be contacted with test substances and the expression of glioma endothelial markers and/or normal endothelial markers determined. Test substances which decrease the expression of glioma endothelial markers (GEMs) are candidates for inhibiting angiogenesis and the growth of tumors. In cases where the activity of a GEM is known, agents can be screened for their ability to decrease or increase the activity.

For those glioma endothelial markers identified as containing transmembrane regions, it is desirable to identify drug candidates capable of binding to the GEM receptors found at the cell surface. For some applications, the identification of drug candidates capable of blocking the GEM receptor from its native ligand will be desired. For some applications, the identification of a drug candidate capable of binding to the GEM receptor may be used as a means to deliver a therapeutic or diagnostic agent. For other applications, the identification of drug candidates capable of mimicking the activity of the native ligand will be desired. Thus, by manipulating the binding of a transmembrane GEM receptor:ligand complex, one may be able to promote or inhibit further development of endothelial cells and hence, vascularization.

For those glioma endothelial markers identified as being secreted proteins, it is desirable to identify drug candidates capable of binding to the secreted GEM protein. For some applications, the identification of drug candidates capable of interfering with the binding of the secreted GEM it is native receptor. For other applications, the identification of drug candidates capable of mimicking the activity of the native receptor will be desired. Thus, by manipulating the binding of the secreted GEM:receptor complex, one may be able to promote or inhibit futher development of endothelial cells, and hence, vascularization.

Expression can be monitored according to any convenient method. Protein or mRNA can be monitored. Any technique known in the art for monitoring specific genes' expression can be used, including but not limited to ELISAs, SAGE, microarray hybridization, Western blots. Changes in expression of a single marker may be used as a criterion for significant effect as a potential pro-angiogenic, anti-angiogenic or anti-tumor agent. However, it also may be desirable to screen for test substances which are able to modulate the expression of at least 5, 10, 15, or 20 of the relevant markers, such as the tumor or normal endothelial markers. Inhibition of GEM protein activity can also be used as a drug screen. Human and mouse GEMS can be used for this purpose.

Test substances for screening can come from any source. They can be libraries of natural products, combinatorial chemical libraries, biological products made by recombinant libraries, etc. The source of the test substances is not critical to the invention. The present invention provides means for screening compounds and compositions which may previously have been overlooked in other screening schemes. Nucleic acids and the corresponding encoded proteins of the markers of the present invention can be used therapeutically in a variety of modes. GEMs can be used to stimulate the growth of vasculature, such as for wound healing or to circumvent a blocked vessel. The nucleic acids and encoded proteins can be administered by any means known in the art. Such methods include, using liposomes, nanospheres, viral vectors, non-viral vectors comprising polycations, etc. Suitable viral vectors include adenovirus, retroviruses, and sindbis virus. Administration modes can be any known in the art, including parenteral, intravenous, intramuscular, intraperitoneal, topical, intranasal, intrarectal, intrabronchial, etc.

Specific biological antagonists of GEMs can also be used to therapeutic benefit. For example, antibodies, T cells specific for a GEM, antisense to a GEM, and ribozymes specific for a GEM can be used to restrict, inhibit, reduce, and/or diminish tumor or other abnormal or undesirable vasculature growth. Such antagonists can be administered as is known in the art for these classes of antagonists generally. Anti-angiogenic drugs and agents can be used to inhibit tumor growth, as well as to treat diabetic retinopathy, rheumatoid arthritis, psoriasis, polycystic kidney disease (PKD), and other diseases requiring angiogenesis for their pathologies.

Mouse counterparts to human GEMS can be used in mouse cancer models or in cell lines or *in vitro* to evaluate potential anti-angiogenic or anti-tumor compounds or therapies. Their expression can be monitored as an indication of effect. Mouse GEMs can be used as antigens for raising antibodies which can be tested in mouse tumor models. Mouse GEMs with transmembrane domains are particularly preferred for this purpose. Mouse GEMs can also be ued as vaccines to raise an immunological response in a human to the human ortholog.

The above disclosure generally describes the present invention. All references disclosed herein are expressly incorporated by reference. A more complete understanding can be obtained by reference to the following specific examples which are provided herein for purposes of illustration only, and are not intended to limit the scope of the invention.

EXAMPLE 1

In this study we employ SAGE transcript profiling to derive the transcriptomes from normal and neoplastic brain tissue. Moreover, we have employed a new version of SAGE, long SAGE, allowing for the derivation of 21 bp SAGE tags. These longer tags allow for the direct interrogation of genomic DNA, identifying unique locations of cell-specific transcription. Endothelial cells from normal brain and different stages of gliomas were expression profiled and compared to each other and to the colon endothelial cell data. Distinct sets of genes define global tumor and normal endothelial cell markers as well as defining glioma-specific endothelial markers. This expanded tumor endothelial cell database will likely provide further insights into the complex regulatory mechanisms governing tumor angiogenesis.

EXAMPLE 2

Tissue procurement and endothelial cell isolation. Five separate brain tissue samples (Table 1) were resected and immediately subjected to endothelial cell isolation with slight modifications to the protocol described previously. St Croix, B., Rago, C., Velculescu, V., Traverso, G., Romans, K. E., Montgomery, E., Lal, A., Riggins, G. J., Lengauer, C., Vogelstein, B., and Kinzler, K. W. (2000). Genes expressed in human tumor endothelium. Science *289*, 1197-202.

Briefly, samples were surgically excised and submerged in DMEM. The samples were minced into 2 centimeter cubes and subjected to tissue digestion with a collagenase cocktail. Samples were mixed at 37°C until dissolved. Cells were spun down and washed two times with PBS/BSA and filtered through successive nylon mesh filters of 250, 100 and 40 microns. Samples were resuspended in PBS/BSA and applied to a 30% Percoll gradient centrifuging for 15 minutes at 800g. 5 ml off the top of the percoll gradient was diluted in 50 ml DMEM and cells pelleted, washed with PBS and resuspended in 3 ml PBS/BSA. Cells were filtered through falcon blue top filter tubes, spun down and resuspended in 1 ml PBS/BSA. 100 microliters of prewashed ant-CD45 magnetic beads (Dynal) were added and the solution allowed to gently mix for ten minutes. Bead-bound cells were discarded and the supernatant transferred to a fresh microcentrifuge tube. 10 microliters of P1H12 mAB (1:100) (Brain N1, T1, and T2 samples) or UEA-I lectin (Brain N2 and T3 samples) was added and the samples were mixed gently at 4°C for 45 minutes. Cells were pelleted and washed 3 times in PBS/BSA and resuspended in 500 microliters PBS/BSA. Prewashed goat anti-mouse M450 dynabeads were added to each tube and allowed to mix for 15 minutes at 4°C. Bead-bound cells were washed 8 times with PBS/BSA and resuspended in a final volume of 500 microliters PBS. Cells were counted and frozen at – 70°C prior to RNA extraction.

EXAMPLE 3

RNA isolation and SAGE library generation. RNA was isolated from the selected cells and initially subjected to RT-PCR analysis to determine the relative abundance of specific, known endothelial cell markers. The microSAGE protocol St Croix, B., Rago, C., Velculescu, V., Traverso, G., Romans, K. E., Montgomery, E., Lal, A., Riggins, G. J., Lengauer, C.,

Vogelstein, B., and Kinzler, K. W. (2000). Genes expressed in human tumor endothelium. Science *289*, 1197-202 (server www, domain name sagenet.org, directory sage_protocol) was used to generate high-quality longSAGE libraries employing the tagging enzyme MmeI instead of BsmFI. 21 base tags were defined by capillary sequencing using a combination of an ABI 3700 and ABI 3100. The sample descriptions and sequencing depth are shown in Table 3.

EXAMPLE 4

Data analysis. Long SAGE tags derived from the brain endothelial samples were reduced to short tags to allow for the integration of colon endothelial SAGE data. Aggregate short tags were derived from the long tags. Any short tag counts that had more than one corresponding long tag representative were summed and the counts represented as one short tag. Both sequencing errors and legitimate long tag derivatives contribute to the generation of multiple long tags. For transcript and genome mapping, differential long tags were employed. Differential gene expression was evaluated as follows: For the two normal brain samples, either the maximum or minimum value was used for determining tumor/normal and normal/tumor ratios, respectively. For the three brain tumor samples, the median value was used for the tumor/normal whereas the maximum value was used for the normal/tumor ratios. A two parameter family of beta distributions was used to assess the probability of observing two fold differences in the observed SAGE tag abundances. Chen, H., Centola, M., Altschul, S. F., and Metzger, H. (1998). Characterization of gene expression in resting and activated mast cells. J Exp Med *188*, 1657-68.

EXAMPLE 5

The following provides a detailed protocol useful for isolating brain endothelial cells. All steps were done at 4° C in cold room and in centrifuge except digestion.

1) Take sample from operating room and submerge in known volume of DMEM+ in 50 ml conical tube to measure tumor volume by displacement. Cut off 2 small pieces of tumor on dry ice and store at –70° C for mRNA extraction/immunohistochemistry/in situ analysis.

2) Take sample from conical and place in small amount of DMEM+ in 10 cm Tissue Culture dish in hood. Mince specimen into 2 mm cubes with sterile scalpel.

3) Transfer minced specimen to small autoclaved erlenmeyer flask and add 5X volume of digestion cocktail. Sample volumes > 5 ml should be split into multiple flasks.

4) Mix in bacterial shaker or in 37° C room on rotating shaker for 45 minutes or until sample is dissolved. Titrate with 10 ml piper every 15 minutes. Once a good cell suspension is obtained, remove and transfer to 50 ml conical.

Remainder of protocol done at 4°C.

5) Spin down at 1500 RPM (600xg) at 4° C for 5 minutes.

6) Wash 2X with PBS/BSA and spin down again. Pool samples.

7) Filter through Nylon Mesh (250, 100, 40 micron).

8) Spin down.

9) Resuspend n PBS/BSA at ½ the original tumor volume.

10) Aply sample in 500 ul aliquots to preformed 30% Percoll gradient (Gradients needed = volume of original sample).

11) Spin at 1750 RPM (800g) for 15 minutes.

12) Remove top 5 ml Percoll from each tube and dilute with DMEM to 50 ml volume.

13) Pellet cells in centrifuge at 1500 RPM. Pool pelleted cells.

14) Wash 2X with PBS/BSA and resuspend in 3 ml PBS/BSA.

15) Filter through Falcon Blue Top Filter tube.

16) Spin down and resuspend in 1 ml PBS/BSA in a 1.5 ml microcentrigufe tube.

17) Add 100 µl of prewashed anti-CD45 beads (hematopoietic depletion) to solution and rotate end over end in cold room for ten minutes. [For brain tissue isolation, an additional negative selection with BerEP4 epithelial depletion is not needed]

18) Remove bead-bound cells and transfer supernatant toa fresh microcentrifuge tube. Save bead-bound sample by freezing at –70° C. Repeat extraction to ensure complete removal of all beads.

19) Add 10 ul of P1H12 mAb (1:100) to cells and mix in cold room with end-over-end roataion for 45 minutes. [As an alternative, selection using UEA1 lectin also provides quality endothelial cell selection.]

20) Pellet cells and wash 3X with PBS/BSA.

21) Resuspend cells in 500 ul of PBS/BSA.

22) Divide sample into four 1.5 ml microcentrifuge tubes (125 ul per tube) and bring volume up to 800 ul. Add 50 ul of prewashed goat anti-mouse M450 dynabeads to each tube.

23) Rotate tubes in cold room for 15 minutes.

24) Separate with magnet and save supernatant as staining control, tumor/brain fraction.

25) Rinse 8X with PBS/BSA.

26) Pool beads into single microcentrifuge tube.

27) Resuspend final cells in 500 ul plain PBS.

28) Take 5 ul of solution and combine with 5 ul of Magic DAPI and count on hemacytometer.

29) Remove 10k cells for staining for quality control based on hemacytometer results

30) Separate beads again and freeze remainder at –70° C for mRNA extraction.

EXAMPLE 6

This example describes the preparation of SAGE tags from mRNA extracted from brain endothelial cells. The preparation is described with reference to standard SAGE tag preparation procedures as are known in the art.

All of the template was used in the PCR SAGE ditag step. Usually we take only a small portion of our template, dilute it and perform ~300 PCR reactions. For these libraries we used all of our material, diluted it and performed ~1200 PCR reactions.

* During the post-amplified PCR product purification step we normally do a standard large volume phenol/chloroform extraction and remove the aqueous layer which contains the product of interest. For these libraries we used Eppendorf's Phase Lock product which creates a physical barrier between the aqueous and organic layers thereby decreasing the amount of product you leave behind. This product was used for all P/C extractions in the second half of the protocol.

* Digesting the amplified PCR products with NlaIII to release the ditag of interest is usually done in one reaction. For these libraries I divided the material into thirds and performed 3 NlaIII reactions in the

hopes of yielding more released ditag.

* Due to the low amount of material, upon entering the concatemer and digested pZERO ligation reaction, I modified the recipe for this reaction to accommodate this. Standard reaction calls for 6ul of concatemers, 2 ul of 5x ligase buffer, 1ul digested pZERO vector, and 1 ul of high concentrate ligase. I modified it to 6ul of concatemers, 2ul of 5x ligase buffer, 0.3-0.5ul of digested pZERO vector, 1 ul high concentrate ligase and filled the missing volume with water. My intention was to favor the concatemer to pZERO ligation reaction relative to the competing pZERO to pZERO ligation reaction.

Most gels during the procedure showed weak amounts of product for visualization and the concatemer gels showed no visible product via the naked eye (we cut out certain fractions regardless).

EXAMPLE 7

Microarray Analysis. Custom 50 nucleotide oligomer arrays were constructed containing 606 unique gene elements. The 606 genes were derived from tumor and normal induced genes from both colon and brain data (328 genes), as well as 278 genes from both literature reviews and housekeeping genes. Arrays were interrogated with Cy3 and Cy5 dye-swapped labelled aRNA samples comparing HMVECs grown on plastic, collagen, fibrin, or Matrigel.

EXAMPLE 8

In situ Hybridizations and Imunohistochemistry. In situ hybridizations for PV I, VEGFR2 and vWF were carried out as desribed previously (10). Co-staining of PV1 and CD31 was carried out as follows: Four 500 nucleotide riboprobe fragments specific for PV1 were transcribed and used to probe formalin fixed 5 micron tissue sections. Final detection of the bound riboprobes were delayed until after the CD31 IHC staining. After PV1 hybridization and washing, tissue sections were fixed for 20 minutes in 4% formaldehyde. After a brief rinse in TBS, antigen retrieval was carried out using DAKO target retrieval solution (DAKO, Cat#S 1699) according to

manufacturer's instructions. After a five minute wash in TBS, slides were digested with Proteinase K at 20 ng/ml in TBS for 20 minutes at 37T, then blocked for 20 minutes at room temperature in block (10% Goat serum/0.5% Casein/0.05% Tween-20/PBS). Slides were incubated with DAKO CD31 (Cat#M0823) at a final concentration of 1 microgram/slide in block solution, for 60 minutes at room temperature. After two 5 minute TBST (DAKO, Cat#S3306) washes at room temperature, PV1 riboprobe and CD31 antibody were detected with Streptavidin-Cy2 (Jackson ImmunoResearch, Cat#016-220-084) at 5 micrograms/slide for the PV1 riboprobe, and goat anti-mouse-Cy3 (Jackson ImmunoResearch, Cat# 115-165 -146) at 2.5 micrograms/slide for CD3 1, for 60 minutes at room temperature. After three Ywashes in TBST, the slides were mounted with antifade medium containing DAPI nuclear counter-stain, cover-slipped and stored at -20'C until viewing. Single images of DAPI, Cy2 and Cy3 images were acquired separately on a Zeiss Axioplan at 40x with a Hammamatsu camera, then merged together to form a composite image using universal imaging metamorph software, and stored at -20C until viewing.

EXAMPLE 9

Capillary-like tubule formation assay. The formation of capillary-like tubular structures was assessed in Matrigel-coated multiwell plates essentially as described previously (12). Briefly, 300 microliters of Matrigel (BD, Bedford, MA) was added to each well of a 24well plate and allowed to polymerize at 37 'C for 30 minutes. HMVECs (BioWhittaker) were infected with adenovius harboring Tem.1 or GFP gene or empty vector (EV) for 67 hours at 300 MOI (Multiplicity Of Infection). Cells were then seeded at a density of 30 x 103 cells/well in 500 microliters EGM-2 medium with supplements (BioWhittaker) in Matrigel-coated plates and incubated at 37 'C for 24 hours and viewed using a Nikon Eclipse TE200 microscope under a phase contrast and photographed. Images were analyzed using software Scion Image (Scion Corporation, Frederick, MD) under the mode of integrated density.

EXAMPLE 9

Cell Proliferation Assay. HMVEC proliferation was assessed by the Cell Titer-Glo Luminescent Cell Viability Assay (Promega, Madison, WI) in 96-well cell culture plates. HMVECs were seeded at 2,000 cells per well in 100 microliters medium and plates were incubated at 37 'C for 48 hours. Reagent was added to each well according to manufacture's instruction, and fluorescence was measured using the Millipore CytoFluor2350.

EXAMPLE 10

Five independent endothelial cell populations were purified from glioma tumor tissue and normal brain tissue. In this study, the tissue defined as normal is derived from patients with epilepsy who have undergone a temporal lobectomy. The samples are summarized in Table 3. Samples N1, T1 and T2 were ultimately P1H12-selected and samples N2 and T3 were UEA-I selected. Prior to SAGE analysis, each sample was assessed for the relative mRNA abundance for vWF, Glial fibrillary acidic protein (GFAP) and EF1 by RT-PCR. Abundant levels of vWF and the control housekeeper EF1, and low levels of the glial cell-specific gene GFAP suggested the cell population was primarily endothelial (data not shown). SAGE analysis was performed to a depth of approximately 50,000 tags (Table 3). For data analysis, each SAGE project was normalized to exactly 50,000 tags. Pairwise comparisons between expression data derived from tumor samples selected with P1H12 or UEA-I showed correlation coefficients around 80%, slightly higher than a comparison between two tumor samples both selected with P1H12. This suggests that selecting endothelial cells with either P1H12 or UEA-I results in highly similar cell populations. Moreover, nearly half of the tumor specific markers revealed in this study are induced 4 fold in each of the normal samples used, suggesting the normal samples are similar populations as well. With this in mind, we felt that combining data for the two normal samples and for the three tumor samples was appropriate.

Table 3. Samples used in this study.

Sample	Description	Tags Generated	EC Selection
Brain N1	Normal temporal lobectomy ECs	43,000	P1H12
Brain N2	Normal temporal lobectomy ECs	49,000	UEA-I
Brain T1	Grade IV Glioma Ecs	46,000	P1H12
Brain T2	Grade III Glioma Ecs	50,000	P1H12
Brain T3	Grade IV Glioma Ecs	58,000	UEA-I
Colon N*	Normal colon Ecs	96,000	P1H12
Colon T*	Tumor colon Ecs	96,000	P1H12
Fetal Brain	Normal bulk	204,000	-
Fetal Kidney	Normal bulk	50,000+	-

Genes specific for endothelial cells showed expression levels consistent with the previously examined colon endothelial SAGE data (Table 4). Additionally, markers specific for epithelial, hematopoeitic or glial cells showed limited or no expression in the brain endothelial libraries suggesting little contamination from non-endothelial cell populations (Table 4). Finally, the data generated here allow for the derivation of a12 gene EC prediction class of which 6 have been previously described as EC-specific (Huminiecki, L., and Bicknell, R. (2000). In silico cloning of novel endothelial-specific genes. Genome Res *10*, 1796-806.) (data not shown). This provides further evidence of pure EC populations used for this study.

Table 4. Cell specificity markers.

Gene	Specificity	Colon N	Colon T	Brain N1	Brain N2	Brain T1	Brain T2	Brain T3
Hevin	EC	161	69	51	99	223	121	48
VWF	EC	35	33	12	53	37	51	110
Tie2/Tek	EC	4	2	2	4	1	4	3
CD34	EC	5	2	3	10	12	4	11
CD14	Hematopoeitic	1	1	1	2	0	0	1
CK8	Epithelial	1	2	0	0	2	1	1
GLUT1	Brain EC	0	1	8	37	2	25	8
GFAP	Glial	0	0	0	0	0	0	0

Genes expressed preferentially in glioma derived endothelial cells as opposed to normal endothelial cells are potentially involved in regulating angiogenesis-dependent tumor growth. Specific parameters for the sorting of SAGE data and the layering of additional statistical filters allowed for a conservative estimate of legitimate differentially expressed genes (see Methods). Excluding mitochondrial genes, 131 genes were observed to be induced in the glioma endothelial cells based on a four fold induction ratio. Only 14 genes can be entertained as glioma-specific when additional statistical filters are applied (Table 5). In this case, a two fold parameter family of distributions was used to estabish a 90% probability of observing at least a 2 fold difference in values. Only one of these twelve genes, apolipoprotein D, shows higher expression in the stage III glioma than at least one of the stage IV tumors. This suggests that many of the highly induced glioma endothelial genes revealed in this analysis may be involved in later stages of angiogenesis where the initiation of vascular sprouting has already occurred or are glioma type specific showing representation in the astrocytoma and not oligodendroglioma-derived ECs.. Less highly induced genes, or genes primarily induced in the less aggressive tumor stage, may be more reflective of angiogenesis initiation. Several genes regulating extracellular matrix architecture are revealed as highly induced in this study. HSPG2 (perlecan), several type IV collagen transcript variants, and matrix metalloprotease 14 (MMP14) have all been shown to play a role in remodeling the extracelullar matrix. Interestingly, other genes that play roles in either cellular signaling or cell-cell communication are also highly expressed exclusively in glioma-associated endothelial cells. Melanoma associated antigen (MG50), endothelin receptor, the G-protein coupled receptor RDC-1, and integrin αV are all cell surface proteins previously demonstrated to play a role in signaling cascades. Although the endothelin receptor, RDC-1 and integrin αV

have previously been shown to regulate angiogenesis, MG50 does not have an association with angiogenesis. Moreover, MG50 was previously shown to be selectively associated with several types of tumor cells with a function yet to be defined. It is noteworthy that the p53-induced, brain-specific angiogenesis inhibitor (BAI-1) was expressed to significant levels but restricted to the earlier stage tumor present in this study (data not shown). It is possible that the loss of expression of BAI-1 in the later tumor stages reflects the need to more aggressively advance vascular development. Other than the detection of a differential HEYL SAGE tag, no other colon endothelial markers were observed to be preferentially expressed in the grade III tumor. In total, of the 14 tumor induced genes listed, 12 are either present on the cell surface or secreted. The localization of the remaining two gene products has yet to be determined as these genes remain uncharacterized. Finally, it is noteworthy that only a select few genes show significant (>2 tags) expression in a fetal brain library where angiogenesis is expected to be robust.

In contrast to the highly biased localization of glioma-induced endothelial cell gene expression defined above, genes that are induced in the normal endothelial cells relative to glioma endothelial cells show a radically different cellular distribution. Twenty-one genes are induced 4 fold or greater in the normal endothelial cells. Filtering for genes with a 50% or greater chance of having greater than 2 fold difference in transcript abundance reduces this list to 14 genes (Table 6). Protein products predicted for these 14 genes show a range of cellular localizations with 4 gene products being intracellular, 5 being integral membrane proteins, 3 extracellular, and one each either secreted, on the cell surface or a nuclear membrane receptor. Several of these genes have functions consistent with either tumor suppressor or anti-angiogenic functions. These anti-proliferative functions have been ascribed to the early growth response gene 1 (EGR1), BTG2, Fruppel-like factor 4 (KLF4), and the serine protease inhibitor SPINT2 although associations with angiogenesis are limited to SPINT2. The down-regulation of these genes in each of the three glioma tumors suggests that these genes may function to encode proteins with anti-angiogenic properties. Both SPINT2 and BTG2 are secreted and may act via paracrine mechanisms. Also noteworthy is the preferential expression of the secreted protein MT1A as this metalothionein may serve as an antioxidant potentially attenuating DNA damage within adjacent cells. Interestingly, EGR1 and KLF4 encode transcription factors suggesting that

some part of the anti-angiogenic pathway revealed here may be initiated by these gene products. With the exception of MT1A, none of the above genes show differential expression in colon tumor ECs and may therefore be glioma-specific EC markers.

The specificity of gene expression for tumor EC subtypes is important to define and can be addressed with the glioma EC data integrated with data obtained previously for colon EC populations. A limited number of genes are preferentially expressed in both brain and colon normal EC populations. In contrast, 16 genes were induced at least 4 fold in both colon and brain tumor EC fractions. 12 of these genes also met the criteria of having a greater than 50% chance of being at least 2 fold differential (Table 7). The majority of these genes (7) are collagen transcripts. However, tumor endothalial marker 1 (TEM1), THY1, and RDC-1 also show consistent induction in the different tumor EC cells. This limited conservation of tumor-induced EC expression suggests highly specific EC expression profiles dependent on the tissue source. TEM1 expression has been validated on tissue arrays harboring tissue slices from astrocytomas (data not shown).

Defining the specificity of gene expression to particular cell types can assist in determining function and designing therapeutics. Our non-endothelial cell SAGE database currently contains 76 libraries encoding 255,000 unique SAGE transcripts. The epithelial cell lines derive from lung, ovary, kidney, prostate, breast, colon, pancreas. Additional non-epithelial sources include cardiomyocytes, melanocytes, glioblastoma and monocytes. Genes which show induction in glioma ECs and demonstrate a restricted expression in non-EC cells may be ideal targets for anti-angiogenic therapies. Allowing for 1 or fewer tags in any non-EC library and at least a four-fold induction in glioma ECs yielded only 5 genes (Table 8). Some of these genes are likely not EC-specific due to the relatively limited number of cell types included within the non-EC database. However, both PV-1 and Plexin A2 (PLXNA2) are interesting genes with potential functional relevance to angiogenesis regulation.

The SAGE tag that defines PLXNA2 falls outside of the current mRNA boundaries residing 3' of the ultimate exon. RT-PCR results, however, have confirmed transcription of

mRNA containing this tag in the tumor samples used to derive the SAGE data. Plexins share homology with the scatter factor/hepatocyte growth factor (SF/HGF) family of receptors encoded by the MET gene family [Tamagnone, L., Artigiani, S., Chen, H., He, Z., Ming, G. I., Song, H., Chedotal, A., Winberg, M. L., Goodman, C. S., Poo, M., Tessier-Lavigne, M., and Comoglio, P. M. (1999). Plexins are a large family of receptors for transmembrane, secreted, and GPI-anchored semaphorins in vertebrates. Cell *99*, 71-80.] Earlier results have demonstrated a link between SF/HGF expression and increase tumorigencity [Bowers, D. C., Fan, S., Walter, K. A., Abounader, R., Williams, J. A., Rosen, E. M., and Laterra, J. (2000). Scatter factor/hepatocyte growth factor protects against cytotoxic death in human glioblastoma via phosphatidylinositol 3-kinase- and AKT- dependent pathways. Cancer Res *60*, 4277-83.] Moreover, SF/HGF promotes this increased tumorigencity with concordant stimulation in angiogenesis [Lamszus, K., Laterra, J., Westphal, M., and Rosen, E. M. (1999). Scatter factor/hepatocyte growth factor (SF/HGF) content and function in human gliomas. Int J Dev Neurosci *17*, 517-30.] In vivo targeting of SF/HGF was demonstrated to inhibit glioma growth and angiogenesis [Abounader, R., Lal, B., Luddy, C., Koe, G., Davidson, B., Rosen, E. M., and Laterra, J. (2002). In vivo targeting of SF/HGF and c-met expression via U1snRNA/ribozymes inhibits glioma growth and angiogenesis and promotes apoptosis. Faseb J *16*, 108-10.]. Plexins are known to function as coreceptors with neuropilin 1 functioning as a receptor for semaphorin and, in turn, regulating neuronal guidance and cell association [Tamagnone, 1999, *supra*]. As neuropilin-1 and Plexin association can serve to receive signals from semaphorins to guide neuronal growth, it is conceivable that a Plexin-neuropilin association may regulate angiogenic growth in a manner analogous to KDR-neuropilin complexes signaling VEGF responses. Plexin A2 shows very low level expression in colon ECs and is not differentially induced in colon tumor ECs. It is noteoworthy that another plexin, plexin B2 (PLXNB2), also showed a five fold increase in glioma EC expression but did not make the statistical threshold demanded for Table 8. Plexin B2 was previously shown to be differentially induced in brain tumors [Shinoura, N., Shamraj, O. I., Hugenholz, H., Zhu, J. G., McBlack, P., Warnick, R., Tew, J. J., Wani, M. A., and Menon, A. G. (1995). Identification and partial sequence of a cDNA that is differentially expressed in human brain tumors. Cancer Lett *89*, 215-21.] The upregulation of plexins in glioma ECs allows for a hypothesis whereby SF/HGF directly stimulates EC migration and proliferation. The novel discovery of a consistently

upregulated level of Plexin A2 in gliomas requires further evidence for a functional link between tumor levels of plexin A2 and angiogenesis regulation, particularly in the brain.

PV-1 (also called PLVAP for plasmallema vesicle associated protein), is a recently discovered type II integral membrane glycoprotein shown to colocalize with caveolin-1. Stan, R. V., Arden, K. C., and Palade, G. E. (2001). cDNA and protein sequence, genomic organization, and analysis of cis regulatory elements of mouse and human PLVAP genes. Genomics *72*, 304-13. Interestingly, this protein was the first to be shown to localize to the stomatal diaphragms and transendothelial channels within caveolae. The specific function of PV-1 remains unknown. PV-1 is expressed at substantial levels in colon ECs but is not expressed differentially between normal and tumor colon ECs. The upregulation of this caveolae-associated protein in gliomas may provide a means for specifically targeting glioma-associated endothelial cells as well as potentially providing a therapeutic delivery mechanism to the underlying tumorigenic cells (Marx, J. (2001). Caveolae: a once-elusive structure gets some respect. Science *294*, 1862-5.))

From this study there is also the potential to define brain EC specific genes irrespective of function or differential expression in normal or tumor tissue. Applying the same criteria as that applied for defining EC restricted glioma induced genes, only two genes, TNFα-induced protein 3 and JUNB, show consistent expression in the brain EC samples but severely limited expression in non-EC databases.

The blood brain barrier within brain capillary endothelial cells results in a restricted diffusion of both small and large molecules as compared to non-brain EC junction complexes. As a result of this, brain capillary ECs facilitate molecular exchange via a tightly regulated, or catalyzed transport system. Any differential expression of catalyzed membrane transporters between normal and tumor tissue may provide a means to selectively deliver therapies to tumor cells. The insulin receptor (IR) has been known for some time to be a marker for brain capillary ECs and to facilitate delivery of drugs. One of the most highly induced, glioma-specific genes in this study is the IR (Table 8). The high induction of IR transcripts in gliomas was not previously

recognized and may provide a selective delivery mechanism to cancer cells as these receptors are also proposed to reside within caveolae structures [Smith, R. M., Jarret, L. (1988). Lab. Invest. *58*, 613-629.] Overall, very few transporters showed a differential induction in glioma-associated ECs as compared to their normal counterpart (Table 9). This is counter to previous suggestions linking altered expression of transporters with histologic grade of CNS tumors [Guerin, C., Wolff, J. E., Laterra, J., Drewes, L. R., Brem, H., and Goldstein, G. W. (1992). Vascular differentiation and glucose transporter expression in rat gliomas: effects of steroids. Ann Neurol *31*, 481-7.] Only one other gene, SLC1A5 Solute carrier family 1 member 5 (neutral amino acid transporter), showed a greater than 4 fold induction in glioma-derived ECs. It should be stated, however, that the standard SAGE tag for integrin αV is shared with aquaporin. Long tag derivations of these two genes revealed that both integrin αV and aquaporin are induced in glioma ECs. Aquaporin may play a role in caveolae swelling that accompanies VEGF stimulated EC growth [Roberts, W. G., and Palade, G. E. (1997). Neovasculature induced by vascular endothelial growth factor is fenestrated. Cancer Res *57*, 765-72.] Only one membrane transporter, Na+/K+ transporting ATP1A2 ATPase, was reciprocally repressed in glioma-derived ECs. It remains possible that certain transporters were missed in this analysis due to incorrect functional assignment. Nonetheless, the low number of differentially regulated transport facilitators suggests a small number of these genes need to be transcriptionally activated to accommodate any necessary increase in protein abundance required for tumor growth.

Table 10 shows genes induced in glioma endothelial cells but not in colon tumor or breast tumor endothelial cells.

Table 11 shows genes which encode transporters which are repressed in glioma endothelial cells.

Table 12 shows genes which encode proteins which are localized to the nucleus of both brain and colon tumor endothelial cells.

Table 13 shows genes which encode proteins which are localized to the cytoplasm of both brain and colon tumor endothelial cells.

Table 14 shows genes which encode proteins which are extracellular from both brain and colon tumor endothelial cells.

Table 15 shows genes which encode proteins which are localized to the membrane of both brain and colon tumor endothelial cells.

Table 16 shows genes which encode proteins which are induced in both brain and colon tumor endothelial cells.

Table 17 shows additional tumor endothelial markers in brain.

Table 18 shows tumor endothelial markers in the brain which are cytoplasmic.

Table 19 shows tumor endothelial markers in the brain which are nuclear.

Table 20 shows tumor endothelial markers in the brain which are membrane associated.

Table 21 shows tumor endothelial markers in the brain which are extracellular.

Table 22 shows tumor endothelial markers in the brain which are unsorted with respect to cellular localization.

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TABLE 5

T/N	T/N prob.	SAGE Tag	UG ID	UG description	localization
17	95	GTCTCAGTGC	118893	Melanoma associated gene MG50	surface/secreted
14	90	CTTATGCTGC	82002	endothelin receptor type B	surface
13	99	CCACCCTCAC	211573	HSPG2 Perlecan	extracellular
13	94	GTGCTACTTC	119129	collagen, type IV, alpha 1	extracellular
12	98	GAGTGAGACC	345643	Thy-1 cell surface antigen	surface
10	94	ATGGCAACAG	149609	ITGA5 integrin alpha 5 (Fn receptor) receptor	surface
9	91	TCACACAGTG	23016	G protein-coupled receptor RDC-1	surface
8	100	GACCGCAGG	119129	collagen, type IV, alpha 1	extracellular
8	97	GGGAGGGGTG	2399	matrix metalloproteinase 14 (membrane-inserted)	extracellular
7	99	CCCTACCCTG	75736	apolipoprotein D	extracellular
6	97	TTCTCCCAAA	75617	collagen, type IV, alpha 2	extracellular
6	98	GGATGCGCAG	302741	Homo sapiens mRNA full length insert cDNA clone EU	
5	98	GTGCTAAGCG	159263	collagen, type VI, alpha 2 Exon 1	extracellular
4	93	CCCAGGACAC	110443	Homo sapiens cDNA: FLJ22215 fis, clone HRC01580.	

TABLE 6

Brain N/T	Brain N/T prob	SAGE Tag	UG ID	UG description	Localization
9	72	TAGTTGGAAA	1119	nuclear receptor subfamily 4, group A, member 1 NR4A1	nuclear membrane
9	72	AAGGGCGCGG	1378	annexin A3 ANXA3	membrane
9	72	AGCTGTGCCA	348254	metallothionein 1A (functional) MT1A	extracellular
7	60	ACAAAATCAA	110613	nuclear pore complex interacting protein SMG-1	membrane
6	68	GCCTGCAGTC	31439	serine protease inhibitor, Kunitz type, 2 SPINT2	extracellular
6	52	ACCAGGTCCA	5167 334549	solute carrier family 5 (sodium-dependent vitamin	membrane
6	52	GGCTAATTAT	34114	ATPase, Na+/K+ transporting, alpha 2 (+) polypepti	membrane
6	75	TTTAAATAGC	7934	KLF4 Kruppel-like factor 4 (gut)	intracellular
5	81	CAGTTCATTA	326035	early growth response 1 EGR1	intracellular
5	61	CTGCCGTGAC	75462	BTG family, member 2 BTG2	extracellular
5	65	TTTTAACTTA	160483	erythrocyte membrane protein band 7.2 (stomatin)	membrane
4	77	TAGAAACCGG	8997	heat shock 70kD protein 1A HSP70	intracellular
4	77	CTTCTTGCC	272572 347939	hemoglobin, alpha 2	intracellular
4	53	TAGAAAAAAT	8906	syntaxin 7	surface

TABLE 7

Brain T/N	colonT/N	SAGE Tag	UG ID	UG description	localization
13	4	GTGCTACTTC	119129	collagen, type IV, alpha 1	extracellular
12	16	GAGTGAGACC	125359	Thy-1 cell surface antigen	surface
9	4	TCACACAGTG	23016	G protein-coupled receptor RDC-1	surface
8	6	GACCGCAGGA	119129	collagen, type IV, alpha 1	extracellular
8	13	GGGAGGGGTG	2399	matrix metalloproteinase 14 (membrane-inserted)	extracellular
7	14	GGGGCTGCCC	195727	tumor endothelial marker 1 precursor	surface
6	4	TTCTCCCAAA	75617	collagen, type IV, alpha 2	extracellular
6	18	CCACAGGGGA	119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrom	extracellular
6	9	TCAAGTTCAC	351928	Homo sapiens mRNA full length insert cDNA Euroimage 1977059	
5	10	ACCAAAAACC	172928	collagen, type I, alpha 1	extracellular
4	7	GATCAGGCCA	119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrom	extracellular
4	4	AGAAACCACG	119129	collagen, type IV, alpha 1	extracellular

TABLE 8

Brain T/N	Brain T/N prob	ShortTag	non-EC count	UG ID	UG description	Localization
9	83	AAGGTTCTTC	1	89695	insulin receptor	surface
7	74	CCCTTTCACA	1	107125	PV1	surface
6	75	AGACTAGGGG	1	350065	Plexin A2	surface
4	69	CATAAACGGG	1	69954	laminin, gamma 3	extracellular
4	53	GGCCAACATT	1	36353	Homo sapiens mRNA full length insert cDNA clone EU	

TABLE 9

Short Tag	Long Tag	UG ID	UG Description
GTACGTCCCA	GTACGTCCCACCCTGTC	183556	solute carrier family 1 (neutral amino acid transp
GCAATTTAAC	GCAATTTAACCACATTT	83974	solute carrier family 21 (prostaglandin transporte
AGGTGCGGGG	AGGTGCGGGGGGCAGAC	165439	arsA (bacterial) arsenite transporter, ATP-binding
TTTGGGGCTG	TTTGGGGCTGGCCTCAC	7476	ATPase, H+ transporting, lysosomal (vacuolar proto
CACCCTGTAC	CACCCTGTACAGTTGCC	25450	solute carrier family 29 (nucleoside transporters)
GGGTGGGCGT	GGGTGGGCGTGCAGGGA	278378	karyopherin beta 2b, transportin

TABLE 10

Unigene ID	Function	LongTag	StdTag	Localization
Hs.101382	tumor necrosis factor, alpha-induced protein 2	ACTCAGCCCGGCTGATG	ACTCAGCCCG	cytoplasmic
Hs.102135	signal sequence receptor, delta (translocon-associated protein delta)	GCTCTCTATGCTGACGT	GCTCTCTATG	membrane
Hs.103180	DC2 protein	AGAATGAAACTGCCGGG	AGAATGAAAC	membrane
Hs.105850	KIAA0404 protein	AAGTGGAATAAACTGCC	AAGTGGAATA	nuclear
Hs.10784	chromosome 6 open reading frame 37	TTTGAATCAGTGCTAGA	TTTGAATCAG	cytoplasmic
Hs.110802	von Willebrand factor	TTCTGCTCTTGTGCCCT	TTCTGCTCTT	extracellular
Hs.112844	maternally expressed 3	TGGGAAGTGGGCTCCTT	TGGGAAGTGG	mitochondria
Hs.11607	hypothetical protein FLJ32205	TGGGCCCGTGTCTGGCC	TGGGCCCGTG	mitochondria
Hs.118893	Melanoma associated gene	ACAACGTCCAGCTGGTG	ACAACGTCCA	extracellular
Hs.119120	E3 ubiquitin ligase SMURF1	CCCCCTGCCCCTCTGCC	CCCCCTGCCC	mitochondria
Hs.121849	microtubule-associated protein 1 light chain 3 beta	GTCTATGCCTCCCAGGA	GTCTATGCCT	nuclear
Hs.124915	hypothetical protein MGC2601	GGCTGGAGCCGCTTTGG	GGCTGGAGCC	extracellular
Hs.129780	tumor necrosis factor receptor superfamily, member 4	CATACCTCCTGCCCCGC	CATACCTCCT	membrane
Hs.135084	cystatin C (amyloid angiopathy and cerebral hemorrhage)	TGCCTGCACCAGGAGAC	TGCCTGCACC	extracellular
Hs.136414	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5	TTCCTTGTAATCAAAGA	TTCCTTGTAA	extracellular
Hs.137574	coagulation factor II (thrombin) receptor-like 3	TGGCGGCAGAGGCAGAG	TGGCGGCAGA	membrane
Hs.148932	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B	CCACGTGGCTGGCTGGG	CCACGTGGCT	membrane
Hs.149152	rhophilin 1	CTGGAGGCTGCCTCGGG	CTGGAGGCTG	nuclear
Hs.149609	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	ATGGCAACAGATCTGGA	ATGGCAACAG	membrane
Hs.151761	KIAA0100 gene product	GGTCCCCTACCCTTCCC	GGTCCCCTAC	nuclear
Hs.155048	Lutheran blood group (Auberger b antigen included)	CCCGCCCCCGCCTTCCC	CCCGCCCCCG	membrane
Hs.155223	stanniocalcin 2	CCCGAGGCAGAGTCGGG	CCCGAGGCAG	extracellular
Hs.155396	nuclear factor (erythroid-derived 2)-like 2	CTACGTGATGAAGATGG	CTACGTGATG	nuclear
Hs.155894	protein tyrosine phosphatase, non-receptor type 1	ATGGGTTTGCATTTTAG	ATGGGTTTGC	cytoplasmic
Hs.155939	inositol polyphosphate-5-phosphatase, 145kDa	ATGGAAGTCTGCGTAAC	ATGGAAGTCT	nuclear
Hs.156351	hypothetical protein FLJ23471	TGGACAGCAGGGACCTG	TGGACAGCAG	nuclear
Hs.1600	chaperonin containing TCP1, subunit 5 (epsilon)	TCATAGAAACCTTGATT	TCATAGAAAC	cytoplasmic
Hs.160958	CDC37 cell division cycle 37 homolog (S. cerevisiae)	CAGCGCTGCATTGACTC	CAGCGCTGCA	cytoplasmic
Hs.165983	zinc finger protein 335	CTGGGTGCCCCAGCCTG	CTGGGTGCCC	nuclear
Hs.169401	apolipoprotein E	CGACCCCACGCCACCCC	CGACCCCACG	extracellular
Hs.172813	Rho guanine nucleotide exchange factor (GEF) 7	CGCTGGGCGTCTGGGAC	CGCTGGGCGT	nuclear
Hs.1735	inhibin, beta B (activin AB beta polypeptide)	ATTAGTCAGAAACTGCC	ATTAGTCAGA	extracellular
Hs.180324	insulin-like growth factor binding protein 5	GATAGCACAGTTGTCAG	GATAGCACAG	extracellular

Unigene ID	Function	LongTag	StdTag	Localization
Hs.180610	splicing factor proline/glutamine rich (polypyrimidine tract binding protein associated)	CGTACTGAGCGCTTTGG	CGTACTGAGC	nuclear
Hs.18069	legumain	GGGGCTTCTGTAGCCCC	GGGGCTTCTG	extracellular
Hs.180842	ribosomal protein L13	CCCGTCCGGAACGTCTA	CCCGTCCGGA	nuclear
Hs.180920	ribosomal protein S9	CCAGTGGCCCGGAGCTG	CCAGTGGCCC	mitochondria
Hs.182248	sequestosome 1	ACTGTACTCCAGCCTAG	ACTGTACTCC	cytoplasmic
Hs.1827	nerve growth factor receptor (TNFR superfamily, member 16)	AGCTCCAGACCCCCAGC	AGCTCCAGAC	membrane
Hs.184245	SMART/HDAC1 associated repressor protein	GACTCGCAGACACCGGG	GACTCGCAGA	nuclear
Hs.184669	zinc finger protein 144 (Mel-18)	GGCCTCCAGCCACCCAC	GGCCTCCAGC	nuclear
Hs.19347	mitochondrial ribosomal protein L45	GACCAGCCTTCAGATGG	GACCAGCCTT	cytoplasmic
Hs.194654	brain-specific angiogenesis inhibitor 1	GCCCCCAGGGGCAGGAC	GCCCCCAGGG	membrane
Hs.19555	prostate tumor over expressed gene 1	GAGGATGGTGTCCTGAG	GAGGATGGTG	cytoplasmic
Hs.195851	actin, alpha 2, smooth muscle, aorta	AAGATCAAGATCATTGC	AAGATCAAGA	cytoplasmic
Hs.201671	SRY (sex determining region Y)-box 13	AGCACAGGGTCGGGGGG	AGCACAGGGT	membrane
Hs.20225	tuftelin interacting protein 11	GCCAAGTGAACTGTGGC	GCCAAGTGAA	cytoplasmic
Hs.202833	heme oxygenase (decycling) 1	CGTGGGTGGGGAGGGAG	CGTGGGTGGG	membrane
Hs.20976	Homo sapiens cDNA FLJ34888 fis, clone NT2NE2017332	CTCCCCTATGGACTGGC	CTCCCCTATG	
Hs.211600	tumor necrosis factor, alpha-induced protein 3	AGTATGAGGAAATCTCT	AGTATGAGGA	nuclear
Hs.212680	tumor necrosis factor receptor superfamily, member 18	GCCCCCTTCCTCCCTTG	GCCCCCTTCC	membrane
Hs.21595	DNA segment on chromosome X and Y (unique) 155 expressed sequence	GGGATTTCTGTGTCTGC	GGGATTTCTG	nuclear
Hs.217493	annexin A2	CTTCCAGCTAACAGGTC	CTTCCAGCTA	nuclear
Hs.2250	leukemia inhibitory factor (cholinergic differentiation factor)	GCCTTGGGTGACAAATT	GCCTTGGGTG	extracellular
Hs.23131	kinesin family member C3	GCCTCCCGCCACGGGGC	GCCTCCCGCC	nuclear
Hs.2340	junction plakoglobin	GTGTGGGGGGCTGGGGG	GTGTGGGGGG	nuclear
Hs.234726	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3	GACTCTTCAGTCTGGAG	GACTCTTCAG	extracellular
Hs.236516	C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9	GCCACACCCACCGCCCC	GCCACACCCA	membrane
Hs.240443	multiple endocrine neoplasia I	CCAGGGCAACAGAATGA	CCAGGGCAAC	nuclear
Hs.25450	solute carrier family 29 (nucleoside transporters), member 1	CACCCTGTACAGTTGCC	CACCCTGTAC	membrane
Hs.25590	stanniocalcin 1	GACGAATATGAATGTCA	GACGAATATG	extracellular
Hs.25590	stanniocalcin 1	CAAACTGGTCTAGGTCA	CAAACTGGTC	extracellular
Hs.25590	stanniocalcin 1	GTAATGACAGATGCAAG	GTAATGACAG	extracellular
Hs.268571	apolipoprotein C-I	TGGCCCCAGGTGCCACC	TGGCCCCAGG	extracellular
Hs.272927	Sec23 homolog A (S. cerevisiae)	AACACAATCATATGATG	AACACAATCA	cytoplasmic
Hs.274184	transcription factor binding to IGHM enhancer 3	GAGGGTATACTGAGGGG	GAGGGTATAC	nuclear
Hs.274453	likely ortholog of mouse embryonic epithelial gene 1	GGAGCCAGCTGACCTGC	GGAGCCAGCT	membrane

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glioma_tem_only_with_tag

Unigene ID	Function	LongTag	StdTag	Localization
Hs.27836	likely ortholog of mouse fibronectin type III repeat containing protein 1	GAGCCTCAGGTGCTCCC	GAGCCTCAGG	membrane
Hs.278573	CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32 and G344)	TACTTCACATACAGTGC	TACTTCACAT	extracellular
Hs.286035	myosin XVB, pseudogene	CGGTGGGACCACCCTGC	CGGTGGGACC	nuclear
Hs.286035	myosin XVB, pseudogene	GGAGAAACAGCTGCTGA	GGAGAAACAG	nuclear
Hs.288203	Homo sapiens, clone IMAGE:4845226, mRNA	GCTCAGGTCTGCCGGGG	GCTCAGGTCT	
Hs.288991	TNFAIP3 interacting protein 2	TCTGCACTGAGAAACTG	TCTGCACTGA	nuclear
Hs.296406	KIAA0685 gene product	TCCACGCCCTTCCTGGC	TCCACGCCCT	nuclear
Hs.29716	hypothetical protein FLJ10980	TTGCAATAGCAAAACCC	TTGCAATAGC	nuclear
Hs.297753	vimentin	TCCAAATCGATGTGGAT	TCCAAATCGA	mitochondria
Hs.29797	ribosomal protein L10	AGGGCTTCCAATGTGCT	AGGGCTTCCA	mitochondria
Hs.299257	ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	AACCTGGGAGGTGGAGG	AACCTGGGAG	
Hs.301242	likely ortholog of mouse myocytic induction/differentiation originator	GGCCAACATTTGGTCCA	GGCCAACATT	cytoplasmic
Hs.301685	KIAA0620 protein	GGGGCTGGAGGGGGGCA	GGGGCTGGAG	membrane
Hs.302741	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 50374	GGATGCGCAGGGGAGGC	GGATGCGCAG	
Hs.318751	ESTs, Weakly similar to T21371 hypothetical protein F25H8.3 - Caenorhabditis elegans [C.elegans]	GAAGACACTTGGTTTGA	GAAGACACTT	
Hs.321231	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 3	GAGAGAAGAGTGATCTG	GAGAGAAGAG	extracellular
Hs.326445	v-akt murine thymoma viral oncogene homolog 2	GCAGGGTGGGGAGGGGT	GCAGGGTGGG	cytoplasmic
Hs.334604	KIAA1870 protein	TCAGTGTATTAAAACCC	TCAGTGTATT	extracellular
Hs.339283	endoplasmic reticulum associated protein 140 kDa	ATACTATAATTGTGAGA	ATACTATAAT	nuclear
Hs.34516	ceramide kinase	GCTGGTTCCTGAGTGGC	GCTGGTTCCT	cytoplasmic
Hs.348000	ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	AGCCACTGCGCCCGGCC	AGCCACTGCG	
Hs.350065	hypothetical protein FLJ30634	AGACTAGGGGCCGGAGC	AGACTAGGGG	nuclear
Hs.352535	KIAA0943 protein	GGGACAGCTGTCTGTGG	GGGACAGCTG	cytoplasmic
Hs.352949	ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	AACCCAGGAGGCGGAGC	AACCCAGGAG	
Hs.353002	ESTs	CAGCCTGAGGCTCTTGG	CAGCCTGAGG	
Hs.353193	LOC124402	CCTCCCCTGCACCTGGG	CCTCCCCTGC	nuclear
Hs.363027	Homo sapiens cDNA FLJ39848 fis, clone SPLEN2014669	GCTTCAGTGGGGGAGAG	GCTTCAGTGG	
Hs.367653	hypothetical protein FLJ22329	TGTTTGGGGGCTTTTAG	TGTTTGGGGG	extracellular
Hs.373548	Homo sapiens cDNA: FLJ22720 fis, clone HSI14320	TTTTAAATTAGGTTTTG	TTTTAAATTA	
Hs.374415	ESTs	ATCTCAAAGATACACAG	ATCTCAAAGA	

Unigene ID	Function	LongTag	StdTag	Localization
Hs.39619	hypothetical protein LOC57333	TTTGTGGGCAGTCAGGC	TTTGTGGGCA	extracellular
Hs.39871	myosin ID	ATTGTAGACAATGAGGG	ATTGTAGACA	nuclear
Hs.400429	ESTs	GCAAAACCCTGCTCTCC	GCAAAACCCT	
Hs.401975	ESTs, Weakly similar to T17346 hypothetical protein DKFZp586O1624.1 - human (fragment) [H.sapiens]	GTCTCAGTGCTGAGGCG	GTCTCAGTGC	
Hs.405289	ESTs, Weakly similar to hypothetical protein FLJ20378 [Homo sapiens] [H.sapiens]	AGCCACTGTGCCCGGCC	AGCCACTGTG	
Hs.406068	ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)	TGATTAAGGTCGGCGCT	TGATTAAGGT	nuclear
Hs.406507	sprouty homolog 4 (Drosophila)	TTACAAACAGAAAAGCT	TTACAAACAG	extracellular
Hs.41716	endothelial cell-specific molecule 1	TTTATTATTGTTCAATA	TTTATTATTG	extracellular
Hs.45008	hypothetical protein DKFZp547N157	CGGGCCTCAGGTGGCAG	CGGGCCTCAG	nuclear
Hs.4980	LIM domain binding 2	TAAAGGCACAGTGGCTC	TAAAGGCACA	nuclear
Hs.5307	synaptopodin	ATATTAGGAAGTCGGGG	ATATTAGGAA	nuclear
Hs.56205	insulin induced gene 1	TGATTAAAACAAGTTGC	TGATTAAAAC	membrane
Hs.57958	EGF-TM7-latrophilin-related protein	TTGTGCACGCATCAGTG	TTGTGCACGC	membrane
Hs.61490	schwannomin interacting protein 1	CCTGCCTCGTAGTGAAG	CCTGCCTCGT	nuclear
Hs.61638	myosin X	CAAAACTGTTTGTTGGC	CAAAACTGTT	nuclear
Hs.62192	coagulation factor III (thromboplastin, tissue factor)	TAGGAAAGTAAAATGGA	TAGGAAAGTA	membrane
Hs.65238	ring finger protein 40	CTCCATCGGCTGTGAGG	CTCCATCGGC	nuclear
Hs.6657	Hermansky-Pudlak syndrome 4	CAAGCATCCCCGTTCCA	CAAGCATCCC	nuclear
Hs.6831	golgi complex associated protein 1, 60kDa	GAGTTAGGCACTTCCTG	GAGTTAGGCA	nuclear
Hs.69954	laminin, gamma 3	CATAAACGGGCACACCC	CATAAACGGG	extracellular
Hs.7187	hypothetical protein FLJ10707	TTGCCTGGGATGCTGGT	TTGCCTGGGA	nuclear
Hs.73798	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	AACGCGGCCAATGTGGG	AACGCGGCCA	cytoplasmic
Hs.73818	ubiquinol-cytochrome c reductase hinge protein	GGTTTGGCTTAGGCTGG	GGTTTGGCTT	nuclear
Hs.74471	gap junction protein, alpha 1, 43kDa (connexin 43)	GATTTTTGTGGTGTGGG	GATTTTTGTG	membrane
Hs.74566	dihydropyrimidinase-like 3	GGCTGCCCTGGGCAGCC	GGCTGCCCTG	cytoplasmic
Hs.74602	aquaporin 1 (channel-forming integral protein, 28kDa)	ATGGCAACAGAAACCAA	ATGGCAACAG	membrane
Hs.75093	procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)	AGAGCAAACCGTAGTCC	AGAGCAAACC	extracellular
Hs.75445	SPARC-like 1 (mast9, hevin)	TGCACTTCAAGAAAATG	TGCACTTCAA	extracellular
Hs.75736	apolipoprotein D	CCCTACCCTGTTACCTT	CCCTACCCTG	extracellular
Hs.76353	serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 5	GGAAAAATGTTGGAATG	GGAAAAATGT	extracellular
Hs.7718	hypothetical protein FLJ22678	GTTTTTGCTTCAGCGGC	GTTTTTGCTT	extracellular
Hs.77313	cyclin-dependent kinase (CDC2-like) 10	GAGGACCCAACAGGAGG	GAGGACCCAA	cytoplasmic
Hs.77326	insulin-like growth factor binding protein 3	ACTGAGGAAAGGAGCTC	ACTGAGGAAA	extracellular
Hs.77573	uridine phosphorylase	TGCAGCGCCTGCGGCCT	TGCAGCGCCT	nuclear

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Unigene ID	Function	LongTag	StdTag	Localization
Hs.77864	KIAA0638 protein	CTGGGGGGAAGGGACTG	CTGGGGGGAA	nuclear
Hs.77886	lamin A/C	GTGCCTGAGAGGCAGGC	GTGCCTGAGA	nuclear
Hs.77886	lamin A/C	TCACAGGGTCCCCGGGG	TCACAGGGTC	nuclear
Hs.77886	lamin A/C	GGAGGGGGCTTGAAGCC	GGAGGGGGCT	nuclear
Hs.78056	cathepsin L	GGAGGAATTCATCTTCA	GGAGGAATTC	extracellular
Hs.78531	similar to RIKEN cDNA 5730528L13 gene	GAAAGTGGCTGTCCTGG	GAAAGTGGCT	nuclear
Hs.78575	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	TCCCTGGCTGTTGAGGC	TCCCTGGCTG	extracellular
Hs.82575	small nuclear ribonucleoprotein polypeptide B"	AAGATGAGGGGGCAGGC	AAGATGAGGG	nuclear
Hs.82749	transmembrane 4 superfamily member 2	CCAACAAGAATGCATTG	CCAACAAGAA	membrane
Hs.83126	TAF11 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 28kDa	AAGGATGCGGTGATGGC	AAGGATGCGG	nuclear
Hs.83169	matrix metalloproteinase 1 (interstitial collagenase)	TGCAGTCACTGGTGTCA	TGCAGTCACT	extracellular
Hs.83384	S100 calcium binding protein, beta (neural)	GCCGTGTAGACCCTAAC	GCCGTGTAGA	cytoplasmic
Hs.83484	SRY (sex determining region Y)-box 4	CAGGCTTTTTGGCTTCC	CAGGCTTTTT	nuclear
Hs.83484	SRY (sex determining region Y)-box 4	TCCCTGGGCAGCTTCAG	TCCCTGGGCA	nuclear
Hs.83727	cleavage and polyadenylation specific factor 1, 160kDa	GAGCGCAGCGAGCTAGC	GAGCGCAGCG	nuclear
Hs.84063	Homo sapiens cDNA: FLJ23507 fis, clone LNG03128	CAGGTGGTTCTGCCATC	CAGGTGGTTC	
Hs.84753	hypothetical protein FLJ12442	GCCCACATCCGCTGAGG	GCCCACATCC	cytoplasmic
Hs.89695	insulin receptor	AAGGTTCTTCTCAAGGG	AAGGTTCTTC	membrane

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Glioma Repressed in Transporters

TABLE 11

Short Tag	Long Tag	UG ID	UG Description
GGCTAATTAT**	GGCTAATTATCATCAAT	34114	ATPase, Na+/K+ transporting alpha 2(+) polypeptide
CAAAAATAAA	CAAAAATAAAAGCCGA	30246	solute carrier family 19 (thiamine transporter), m
			Transport
**Also present in Glioma repressed list			

TABLE 12

Nuclear Brain and Colon Proteins

Unigene ID	Function	OMIM ID	Protein
Hs.149098	smoothelin	602127	NP_599031
Hs.197298	NS1-binding protein		AAG43485
Hs.337986	hypothetical protein MGC4677		NP_443103

TABLE 13

Cytoplasmic Brain/Colon Proteins

Unigene ID	Function	OMIM ID	Protein
Hs.327412	TEM 15, COL3A1, Homo sapiens clone FLC1492 PRO3121 mRNA, complete cds		
Hs.75721	profilin 1	176610	NP_005013

TABLE 14

Extracellular Colon/Brain Proteins

Unigene ID	Function	OMIM ID	Protein
Hs.1103	transforming growth factor, beta 1 (Camurati-Engelmann disease)	190180	NP_000651
Hs.111779	secreted protein, acidic, cysteine-rich (osteonectin)	182120	NP_003109
Hs.119129	collagen, type IV, alpha 1	120130	NP_001836
Hs.119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant	120180	NP_000081
Hs.151738	matrix metalloproteinase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	120361	NP_004985
Hs.159263	collagen, type VI, alpha 2	120240	NP_001840
Hs.172928	collagen, type I, alpha 1	120150	NP_000079
Hs.179573	TEM 40, COL1A2 alt polyA; involved in tissue remodeling	120160	NP_000080

Unigene ID	Function	OMIM ID	Protein
Hs.75617	collagen, type IV, alpha 2	120090	NP_001837
Hs.78672	laminin, alpha 4	600133	NP_002281
Hs.821	biglycan	301870	NP_001702

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TABLE 15

Membrane Brain/Colon Proteins

Unigene ID	Function	OMIMID	Protein
Hs.125359	TEM 13, Thy-1 cell surface antigen	188230	NP_006279
Hs.185973	degenerative spermatocyte homolog, lipid desaturase (Drosophila)		NP_003667
Hs.195727	TEM 1, endosialin	606064	NP_065137
Hs.23016	G protein-coupled receptor		
Hs.2399	matrix metalloproteinase 14 (membrane-inserted)	600754	NP_004986
Hs.285814	sprouty homolog 4 (Drosophilia)		AAK00653
Hs.82002	endothelin receptor type B	131244	NP_000106

TABLE 16

Brain and Colon Proteins

Unigene ID	Function	OMIM ID	Protein
Hs.1103	transforming growth factor, beta 1 (Camurati-Engelmann disease)	190180	NP_000651
Hs.111779	secreted protein, acidic, cysteine-rich (osteonectin)	182120	NP_003109
Hs.119129	collagen, type IV, alpha 1	120130	NP_001836
Hs.119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)	120180	NP_000081
Hs.125359	TEM 13, Thy-1 cell surface antigfen	188230	NP_006279
Hs.149098	smoothelin	602127	NP_599031
Hs.151738	matrix metalloproteinase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	120361	NP_004985
Hs.159263	collagen, type VI, alpha 2	120240	NP_001840

Unigene ID	Function	OMIMID	Protein
Hs.172928	collagen, type 1, alpha 1	120150	NP_000079
Hs.179573	TEM 40, COL1A2 alt polyA; involved in tissue remodeling	120160	NP_000080
Hs.185973	degenerative spermatocyte homolog, lipid desaturase (Drosophila)		NP_003667
Hs.195727	TEM 1, endosialin	606064	NP_065137
Hs.197298	NS1-binding protein		AAG43485
Hs.23016	G protein-coupled receptor		
Hs.2399	matrix metalloproteinase 14 (membrane-inserted)	600754	NP_004986
Hs.285814	sprouty homolog 4 (Drosophila)		AAK00653
Hs.327412	TEM15, COL311, Homo sapiens clone FLC1492 PRO3121 mRNA, complete cds		
Hs.337986	hypotehtical protein MGC4677		NP_443103
Hs.351928	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1977059		

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Unigene ID	Function	OMIMID	Protein
Hs.356096	ESTs, Highly similar to hypothetical protein FLJ10350 [Homo sapiens] [H.sapiens]		
Hs.75617	collagen, type IV, alpha 2	120090	NP_001837
Hs.75721	profilin 1	176610	NP_005013
Hs.78672	laminin, alpha 4	600133	NP_002281
Hs.82002	endothelin receptor type B	131244	NP_000106
Hs.821	biglycan	301870	NP_001702

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TABLE 17

Additional Tumor Endothelial Markers in Brain

Unigene ID	Function	
Hs.326445	v-akt murine thymoma vial oncogene homolog 2	Protein Kinase
Hs. 77313	cyclin-dependent kinase (cdc2-like) 10	Protein Kinase
Hs.301242	ortholog mouse myocytic induction/differntiation originator	Non-Protein Kinase
Hs.194654	brain-specific angiogenesis inhibitor 1	Membrane GPCR
Hs.57958	EGF-RM7 latrophilin-related protein	Membrane GPCR
Hs.148932	sema domain	Receptors with Short Cytoplasmic Tail

Unigene ID	Function	
Hs.149609	integrin, alpha 5	Receptors with Short Cytoplasmic Tail
Hs.27836	likely ortholog of mouse fibronectin type III	Receptors with Short Cytoplasmic Tail
Hs.155048	Lutheran blood group (Auberger b antigen included)	Receptors with Short Cytoplasmic Tail
Hs.102135	SSR4, TRAPD	Receptors with Short Cytoplasmic Tail
Hs.1827	nerve growth factor receptor (TNFR superfamily, member 16)	Membrane Receptor
Hs.41716	insulin-like growth factor binding protein	Extracellular Growth Factors & Cytokine
Hs.2250	leukemia inhibitor factor	Extracellular Growth Factors & Cytokine
Hs.155894	protein typrosine phosphatase, nonreceptor type I	Cell-Selective Phosphatase

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TABLE 18

Cytoplasmic GEMs

Unigene ID	Function	OMIMID	Protein
Hs.111611	ribosomal protein L27	607526	NP_000979
Hs.160958	CDC37 cell division cycle 37 homolog (S. cerevisiae)	605065	NP_008996
Hs.327412	TEM15, COLI3A1, Homo sapiens clone FLC1492 PRO3121 mRNA, complete cds		
Hs.34516	ceramide kinase		NP_073603
Hs.352535	KIAA0943 protein		BAA76787
Hs.61661	F-box only protein 32	606604	NP_478136
Hs.73798	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	153620	NP_002406
Hs.75721	profilin 1	176610	NP_005013
Hs.83384	S100 calcium binding protein, beta (neural)	176990	NP_006263

TABLE 19. Nuclear GEMs

Unigene ID	Function	OMIMID	Protein
Hs.105850	KIAA0404 protein		BAA23700
Hs.110443	hypothetical protein FLJ22215		NP_073745
Hs.121849	microtubule-associated protein 1 light chain 3 beta		NP_073729
Hs.129673	eukaryotic translation initiation factor 4A, isoform 1	602641	NP_001407
Hs.149098	smoothelin	602127	NP_599031
Hs.155396	nuclear factor (erythroid-derived 2)-like 2	600492	NP_006155
Hs.172813	Rho guanine nucleotide exchange factor (GEF) 7	605477	NP_663788
Hs.197298	NS1-binding protein		AAG43485
Hs.211600	tumor necrosis factor, alpha-induced protein 3	191163	NP_006281
Hs.217493	annexin A2	151740	—
Hs.2340	junction plakoglobin	173325	NP_002221
Hs.274184	transcription factor binding to IGHM enhancer 3	314310	NP_006512
Hs.286035	myosin XVB, pseudogene		
Hs.332173	transducin-like enhancer of split 2 (E(sp1) homolog, Drosophila)	601041	NP_003251
Hs.337986	hypothetical protein MGC4677		NP_443103
Hs.339283	endoplasmic reticulum associated protein 140 kDa		
Hs.350065	hypothetical protein FLJ30634		NP_694559
Hs.65238	ring finger protein 40		NP_055586
Hs.6657	Hermansky-Pudlak syndrome 4	606682	BAB33337
Hs.75061	MARCKS-like protein	602940	NP_075385
Hs.77573	uridine phosphorylase	191730	NP_003355
Hs.77886	lamin A/C	150330	NP_005563

TABLE 20. Membrane GEMs

Unigene ID	Function	OMIMID	Protein
Hs.107125	plasmalemma vesicle associated protein		NP_112600
Hs.125359	TEM13, Thy-1 cell surface antigen	188230	NP_006279
Hs.137574	coagulation factor II (thrombin) receptor-like 3	602779	NP_003941
Hs.143897	dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)	603009	NP_003485
Hs.148932	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B		NP_115484
Hs.149609	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	135620	NP_002196
Hs.166254	likely ortholog of rat vacuole membrane protein 1		NP_112200
Hs.1827	nerve growth factor receptor (TNFR superfamily, member 16)	162010	NP_002498
Hs.185973	degenerative spermatocyte homolog, lipid desaturase (Drosophila)		NP_003667
Hs.195727	TEM1, endosialin	606064	NP_065137
Hs.202833	heme oxygenase (decycling) 1	141250	NP_002124
Hs.23016	G protein-coupled receptor		
Hs.236516	C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9		NP_055173
Hs.2399	matrix metalloproteinase 14 (membrane-inserted)	600754	NP_004986
Hs.25450	solute carrier family 29 (nucleoside transporters), member 1	602193	NP_004946
Hs.274453	likely ortholog of mouse embryonic epithelial gene 1		NP_060081

TABLE 20. Membrane GEMs (pg. 2)

Unigene ID	Function	OMIMID	Protein
Hs.277477	major histocompatibility complex, class I, C	142840	NP_00210 8
Hs.27836	likely ortholog of mouse fibronectin type III repeat containing protein 1		NP_07373 4
Hs.285814	sprouty homolog 4 (Drosophila)		AAK00653
Hs.301685	KIAA0620 protein		BAA31595
Hs.62192	coagulation factor III (thromboplastin, tissue factor)	134390	NP_00198 4
Hs.74602	aquaporin 1 (channel-forming integral protein, 28kDa)	110450	AAH2248 6
Hs.77961	major histocompatibility complex, class I, B	142830	NP_00550 5
Hs.79356	Lysosomal-associated multispanning membrane protein-5	601476	NP_00675 3
Hs.82002	endothelin receptor type B	131244	NP_00010 6
Hs.89695	insulin receptor	147670	NP_00019 9
Hs.97199	complement component 1, q subcomponent, receptor 1	120577	NP_03620 4

TABLE 21. Extracellular GEMS

Unigene ID	Function	OMIMID	Protein
Hs.1103	transforming growth factor, beta 1 (Camurati-Engelmann disease)	190180	NP_000651
Hs.110802	von Willebrand factor	193400	NP_000543
Hs.111779	secreted protein, acidic, cysteine-rich (osteonectin)	182120	NP_003109
Hs.119129	collagen, type IV, alpha 1	120130	NP_001836
Hs.119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)	120180	NP_000081
Hs.135084	cystatin C (amyloid angiopathy and cerebral hemorrhage)	604312	NP_000090
Hs.136414	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5		NP_114436
Hs.151738	matrix metalloproteinase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	120361	NP_004985
Hs.159263	collagen, type VI, alpha 2	120240	NP_001840
Hs.169401	apolipoprotein E	107741	NP_000032
Hs.172928	collagen, type I, alpha 1	120150	NP_000079
Hs.1735	inhibin, beta B (activin AB beta polypeptide)	147390	NP_002184
Hs.179573	TEM40, COL1A2 alt polyA; involved in tissue remodeling	120160	NP_000080
Hs.180324	insulin-like growth factor binding protein 5	146734	
Hs.18069	legumain	602620	NP_005597
Hs.211573	heparan sulfate proteoglycan 2 (perlecan)	142461	NP_005520
Hs.25590	stanniocalcin 1	601185	NP_003146
Hs.268571	apolipoprotein C-I	107710	
Hs.321231	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 3	604014	NP_003770
Hs.365706	matrix Gla protein	154870	NP_000891
Hs.367653	hypothetical protein FLJ22329		
Hs.69954	laminin, gamma 3	604349	NP_006050
Hs.73817	chemokine (C-C motif) ligand 3	182283	NP_002974
Hs.75111	protease, serine, 11 (IGF binding)	602194	NP_002766
Hs.75445	SPARC-like 1 (mast9, hevin)	606041	NP_004675
Hs.75617	collagen, type IV, alpha 2	120090	NP_001837
Hs.75736	apolipoprotein D	107740	NP_001638

TABLE 21. Extracellular GEMs (pg. 2)

Unigene ID	Function	OMIMID	Protein
Hs.7718	hypothetical protein FLJ22678		NP_078812
Hs.77326	insulin-like growth factor binding protein 3	146732	NP_000589
Hs.78575	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	176801	NP_002769
Hs.78672	laminin, alpha 4	600133	NP_002281
Hs.82085	serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	173360	NP_000593
Hs.821	biglycan	301870	NP_001702
Hs.83169	matrix metalloproteinase 1 (interstitial collagenase)	120353	NP_002412
Hs.90107	adhesion regulating molecule 1		NP_008933

TABLE 22. Brain tumor markers unsorted

Unigene ID	Function	OMIMID	Protein
Hs.105850	KIAA0404 protein		BAA23700
Hs.107125	plasmalemma vesicle associated protein		NP_112600
Hs.1103	transforming growth factor, beta 1 (Camurati-Engelmann disease)	190180	NP_000651
Hs.110443	hypothetical protein FLJ22215		NP_073745
Hs.110802	von Willebrand factor	193400	NP_000543
Hs.111611	ribosomal protein L27	607526	NP_000979
Hs.111779	secreted protein, acidic, cysteine-rich (osteonectin)	182120	NP_003109
Hs.11607	hypothetical protein FLJ32205		NP_689774
Hs.119129	collagen, type IV, alpha 1	120130	NP_001836
Hs.119571	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)	120180	NP_000081
Hs.121849	microtubule-associated protein 1 light chain 3 beta		NP_073729
Hs.125359	TEM13, Thy-1 cell surface antigen	188230	NP_006279
Hs.127824	ESTs, Weakly similar to CA28_HUMAN Collagen alpha 2(VIII) chain (Endothelial collagen) [H.sapiens]		
Hs.129673	eukaryotic translation initiation factor 4A, isoform 1	602641	NP_001407
Hs.135084	cystatin C (amyloid angiopathy and cerebral hemorrhage)	604312	NP_000090
Hs.136414	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5		NP_114436
Hs.137574	coagulation factor II (thrombin) receptor-like 3	602779	NP_003941
Hs.143897	dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)	603009	NP_003485
Hs.148932	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B		NP_115484
Hs.149098	smoothelin	602127	NP_599031
Hs.149609	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	135620	NP_002196

TABLE 22. Brain tumor markers unsorted (pg. 2)

Unigene ID	Function	OMIMID	Protein
Hs.151738	matrix metalloproteinase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	120361	NP_004985
Hs.155396	nuclear factor (erythroid-derived 2)-like 2	600492	NP_006155
Hs.159263	collagen, type VI, alpha 2	120240	NP_001840
Hs.160958	CDC37 cell division cycle 37 homolog (S. cerevisiae)	605065	NP_008996
Hs.166254	likely ortholog of rat vacuole membrane protein 1		NP_112200
Hs.169401	apolipoprotein E	107741	NP_000032
Hs.172813	Rho guanine nucleotide exchange factor (GEF) 7	605477	NP_663788
Hs.172928	collagen, type I, alpha 1	120150	NP_000079
Hs.1735	inhibin, beta B (activin AB beta polypeptide)	147390	NP_002184
Hs.179573	TEM40, COL1A2 alt polyA; involved in tissue remodeling	120160	NP_000080
Hs.180324	insulin-like growth factor binding protein 5	146734	
Hs.18069	legumain	602620	NP_005597
Hs.180920	ribosomal protein S9	603631	
Hs.1827	nerve growth factor receptor (TNFR superfamily, member 16)	162010	NP_002498
Hs.185973	degenerative spermatocyte homolog, lipid desaturase (Drosophila)		NP_003667
Hs.195727	TEM1, endosialin	606064	NP_065137
Hs.197298	NS1-binding protein		AAG43485
Hs.202833	heme oxygenase (decycling) 1	141250	NP_002124
Hs.20976	Homo sapiens cDNA FLJ34888 fis, clone NT2NE2017332		
Hs.211573	heparan sulfate proteoglycan 2 (perlecan)	142461	NP_005520
Hs.211600	tumor necrosis factor, alpha-induced protein 3	191163	NP_006281
Hs.217493	annexin A2	151740	
Hs.23016	G protein-coupled receptor		
Hs.2340	junction plakoglobin	173325	NP_002221
Hs.236516	C-type (calcium dependent, carbohydrate-recognition domain) lectin, superfamily member 9		NP_055173
Hs.2399	matrix metalloproteinase 14 (membrane-inserted)	600754	NP_004986

TABLE 22. Brain tumor markers unsorted (pg. 3)

Unigene ID	Function	OMIMID	Protein
Hs.25450	solute carrier family 29 (nucleoside transporters), member 1	602193	NP_004946
Hs.26590	stanniocalcin 1	601185	NP_003146
Hs.268571	apolipoprotein C-I	107710	
Hs.274184	transcription factor binding to IGHM enhancer 3	314310	NP_006512
Hs.274453	likely ortholog of mouse embryonic epithelial gene 1		NP_060081
Hs.277477	major histocompatibility complex, class I, C	142840	NP_002108
Hs.27836	likely ortholog of mouse fibronectin type III repeat containing protein 1		NP_073734
Hs.285814	sprouty homolog 4 (Drosophila)		AAK00653
Hs.286035	myosin XVB, pseudogene		
Hs.288203	Homo sapiens, clone IMAGE:4845226, mRNA		
Hs.29797	ribosomal protein L10	312173	NP_115617
Hs.299257	ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]		
Hs.301685	KIAA0620 protein		BAA31595
Hs.302741	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 50374		
Hs.318751	ESTs, Weakly similar to T21371 hypothetical protein F25H8.3 - Caenorhabditis elegans [C.elegans]		
Hs.321231	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 3	604014	NP_003770
Hs.327412	TEM15, COL3A1, Homo sapiens clone FLC1492 PRO3121 mRNA, complete cds		
Hs.332173	transducin-like enhancer of split 2 (E(sp1) homolog, Drosophila)	601041	NP_003251
Hs.337986	hypothetical protein MGC4677		NP_443103
Hs.339283	endoplasmic reticulum associated protein 140 kDa		
Hs.34516	ceramide kinase		NP_073603
Hs.350065	hypothetical protein FLJ30634		NP_694559

TABLE 22. Brain tumor markers unsorted (pg. 4)

Unigene ID	Function	OMIMID	Protein
Hs.351928	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1977059		
Hs 352535	KIAA0943 protein		BAA76787
Hs.352949	ESTs, Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]		
Hs 356096	ESTs, Highly similar to hypothetical protein FLJ10350 [Homo sapiens] [H.sapiens]		
Hs.363027	Homo sapiens cDNA FLJ39848 fis, clone SPLEN2014669		
Hs.365706	matrix Gla protein	154870	NP_000891
Hs.367653	hypothetical protein FLJ22329		
Hs.374415	ESTs		
Hs.380983	ESTs, Highly similar to ITB1_HUMAN Integrin beta-1 precursor (Fibronectin receptor beta subunit) (CD29) (Integrin VLA-4 beta subunit) [H.sapiens]		
Hs.400429	ESTs		
Hs.401975	ESTs, Weakly similar to T17346 hypothetical protein DKFZp586O1624.1 - human (fragment) [H.sapiens]		
Hs.61661	F-box only protein 32	606604	NP_478136
Hs.62192	coagulation factor III (thromboplastin, tissue factor)	134390	NP_001984
Hs.65238	ring finger protein 40		NP_055586
Hs.6657	Hermansky-Pudlak syndrome 4	606682	BAB33337
Hs.69954	laminin, gamma 3	604349	NP_006050
Hs.73798	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	153620	NP_002406
Hs.73817	chemokine (C-C motif) ligand 3	182283	NP_002974
Hs.74602	aquaporin 1 (channel-forming integral protein, 28kDa)	110450	AAH22486
Hs.75061	MARCKS-like protein	602940	NP_075385
Hs.75111	protease, serine, 11 (IGF binding)	602194	NP_002766

TABLE 22. Brain tumor markers unsorted (pg. 5)

Unigene ID	Function	OMIMID	Protein
Hs.75445	SPARC-like 1 (mast9, hevin)	606041	NP_004675
Hs.75617	collagen, type IV, alpha 2	120090	NP_001837
Hs.75721	profilin 1	176610	NP_005013
Hs.75736	apolipoprotein D	107740	NP_001638
Hs.7718	hypothetical protein FLJ22678		NP_078812
Hs.77326	insulin-like growth factor binding protein 3	146732	NP_000589
Hs.77573	uridine phosphorylase	191730	NP_003355
Hs.77886	lamin A/C	150330	NP_005563
Hs.77961	major histocompatibility complex, class I, B	142830	NP_005505
Hs.78575	prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)	176801	NP_002769
Hs.78672	laminin, alpha 4	600133	NP_002281
Hs.79356	Lysosomal-associated multispanning membrane protein-5	601476	NP_006753
Hs.82002	endothelin receptor type B	131244	NP_000106
Hs.82085	serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	173360	NP_000593
Hs.821	biglycan	301870	NP_001702
Hs.83169	matrix metalloproteinase 1 (interstitial collagenase)	120353	NP_002412
Hs.83384	S100 calcium binding protein, beta (neural)	176990	NP_006263
Hs.84063	Homo sapiens cDNA: FLJ23507 fis, clone LNG03128		
Hs.89695	insulin receptor	147670	NP_000199
Hs.90107	adhesion regulating molecule 1		NP_008933
Hs.97199	complement component 1, q subcomponent, receptor 1	120577	NP_036204